



# Increasing awareness of available resources for mitigating risk in Long QT and Brugada Syndromes.

Marnie ODonnell PAC, Jason Imundo MD

Pediatric Cardiology Electrophysiology, Penn State Hershey Medical Center, Hershey, PA

Sudden cardiac death (SCD) usually occurs in patients with **structural heart disease in over 80% of the incidents.**  
-There has been increase in the understanding of sudden cardiac death and cardiac arrest in **structurally normal hearts.**  
-Often due to underlying ion channelopathy syndromes.<sup>1</sup> These are syndromes caused by disturbed function of ion channels and their proteins.<sup>2</sup>

**Long QT Syndrome and Brugada Syndrome are two such diseases.**  
-Extrinsic factors, **especially drugs**, modulate ion channels.  
-Life threatening arrhythmias can be triggered by the use of these drugs.<sup>4</sup>

This occurs in:  
-Underlying syndromes  
-Acquired syndromes due to the use of particular drugs<sup>3</sup>

**Websites exist to reference drugs of caution.**  
They provide access to lists of drugs in **one location.**  
These sites help to avoid dangerous drugs for affected patients.<sup>4</sup>

**The websites are:**  
-Free  
-Available worldwide

**Advisory boards exist for each site.**  
They provide recommendations from experts in the field.  
-Advisory Boards are highly respected clinical/basic scientists.  
-Board activities about the drug lists:  
  Consultation & Aid decision making

**Decisions are made based on:**  
-their experience  
-interpretation of summaries of the latest evidence acquired  
-data in publication of new evidence in literature/case reports  
-laboratory studies  
-cohort analysis

Consensus recommendations can be made by the Advisory boards. Changes can be made to the websites within a few weeks.<sup>1</sup>

**Both websites provide free registration to receive updates in your email.**

**The following information provides examples of the information and the icons that will be found on the separate websites provided to you here so you will be comfortable when you visit the sites.**


**QT drug list:**<sup>5</sup>  
<https://www.crediblemeds.org>  
Developed in 2001.  
Medications listed that can prolong the QT interval on the ECG.  
There is the risk of the potentially lethal ventricular arrhythmia Torsade de Pointes (TdP).  
**Both generic name and brand names are listed.**  
**Available in English & Spanish.**

 **Known Risk of TdP**


Prolong the QT interval & have risk of causing the potentially lethal ventricular arrhythmia TdP  
-This risk is different for each drug & people have different levels of sensitivity to the effects of these drugs on the heart **Examples: azithromycin, erythromycin, ciprofloxacin, escitalopram, fluconazole, ondansetron**

 **Possible Risk of TdP**

Prolongs the QT interval on EKG but lack substantial evidence that they can cause TdP  
-Generally the FDA discourages two or more drugs that can prolong the QT interval b/c of the increased risk of TdP. **Examples: promethazine, lithium, nortriptyline, atomoxetine, hydrocodone, levetiracetam**

 **Conditional Risk of TdP**

Risk of TdP or excess QT prolonging under certain conditions. Conditions include:  
-inhibiting metabolism of a QT prolonging drug  
-creating electrolyte disturbance  
-drug overdose  
-co administration of potential interacting drugs. (Otherwise these drugs lack substantial evidence that they can cause TdP. ) **Examples: sertraline, famotidine, omeprazole, furosemide, diphenhydramine**

 **Drugs to avoid in Congenital Long QT**

**Examples: sulfamethoxazole & trimethoprim, albuterol, methylphenidate, pseudoephedrine**

**Brugada drug list:**<sup>6</sup>  
<https://www.brugadadrugs.org>  
Created in 2009.  
List identifies potential harm with certain drugs.  
**Both generic name and brand names are listed.**  
**Available in 25 languages.**

**Drugs to be avoided**

On this list is summarized those drugs for which there is literature available for an association btw the drug and arrhythmias in Brugada Syndrome.  
**Examples: Amitriptyline, procaine, propofol, lithium, procaine, bupivacaine, cannabis**

**Drugs preferentially avoided**

The following drugs have been associated with the typical (type-1) Brugada syndrome ECG. However, there is (yet) no substantial evidence that these drugs can, in addition to the ECG phenotype, also cause malignant arrhythmias.  
**Examples: lidocaine, propranolol, verapamil, bupropion, fluoxetine, lamotrigine, paroxetine, diphenhydramine, metoclopramide**

**Patient letter**

**A letter listing all the drugs to avoid in Brugada Syndrome can be printed and given to their Healthcare providers.**

The drug lists are updated every 30-60 days due to constant review of scientific literature, FDA announcements & case reports. It is beneficial to register your email to receive updates & notices. <sup>5</sup>

**To see the ENTIRE listing of medications to be used with caution: Go to the Websites.**

**Limitations of the Websites**  
-Patients with the channelopathies have varying underlying levels of risk of developing arrhythmias when taking drugs.  
-None of the drugs listed will have the same impact for all patients.  
-Negative impact of patients not receiving potentially effective treatments due to reluctance of physicians to prescribe medications or patient refusal b/c it's on the website. Clinical judgement is needed and the websites cannot replace those judgements.  
This means risk assessment and stratification is heavily relied on; although it sometimes disputed among experts.<sup>1</sup>

**Significant limitation is:**  
These websites are only of use to those who are aware of their existence.<sup>1</sup>

**References**  
1. Nabil El Sheriff, Mohamed Boutjdir (2015). Role of pharmacotherapy in cardiac ion channelopathies. Pharmacology & Therapeutics 155 ,132-142.  
2. Wikipedia: <https://en.m.wikipedia.org>  
3. Isik,Turker, Tomohiko Ai, Hideki Itoh, Minoru Horie (2017). Drug-Induced fatal arrhythmias: Acquired long QT and Brugada syndromes. Pharmacology & Therapeutics 176 (48-59).  
4. Pieter Postema, Jon Neville, Jonas S.S.G. de Jong, Klaus Romero, Arthur A.M. Wilde, and Raymond L. Woosley (2013). Safe drug use in long QT syndrome and Brugada syndrome: comparison of website statistics. Europace 15, 1042-1049.  
5. <https://www.crediblemeds.org>  
6. <https://www.brugadadrugs.org>  
7. Picture available from PennLive

**Title:** Increasing awareness of available resources for mitigating risk in Long QT and Brugada Syndromes

**Authors:** Marnie O'Donnell PAC, Jason Imundo MD

**Introduction:** Sudden cardiac death (SCD) usually occurs in patients with organic heart disease in over eighty percent of the incidents. In recent years there has been significant increase in the understanding of sudden cardiac death and cardiac arrest in structurally normal hearts. This frequently occurs in the young as a result of underlying ion channelopathy syndromes.<sup>1</sup> These channelopathy syndromes are diseases caused by disturbed function of ion channel subunits or the proteins that regulate them.<sup>2</sup>

Among these syndromes, Long QT Syndrome and Brugada Syndrome are two of them. The malfunction of ion channels is intrinsic in these syndromes and it has been recognized that extrinsic factors, especially drugs, can modulate cardiac ion channel function and even result in dysfunction. This can occur for those who have these underlying syndromes as well as for those with acquired forms of these syndromes due to the use of particular drugs.<sup>3</sup> Life threatening arrhythmias can be triggered by the use of these particular drugs.<sup>4</sup>

**Methods:** Literature search and review of the websites as referenced

**Results:** There are two separate websites that exist that provides reference of the drugs that caution needs to be taken for Long QT Syndrome and Brugada Syndrome; they are [crediblemeds.org](http://crediblemeds.org)<sup>5</sup> and [brugadadrugs.org](http://brugadadrugs.org)<sup>6</sup> respectively. These websites exist for medical professionals and patients to have access to lists of drugs in one location so precaution can be taken when choosing medications for affected individuals. This is important to avoid potentially life threatening arrhythmias in these group of patients. <sup>4</sup>

**Conclusion:** The purpose of this project is to increase awareness of these websites. These websites provide free and worldwide availability of information on drug safety in these syndromes and for those with drug acquired electrocardiogram abnormalities. There are advisory boards for each site to be able to provide consensus recommendations from experts in the field. <sup>4</sup> This project provides information about the websites and an explanation about the drug categories.

#### References

1. Nabil El-Sherif, Mohamed Boutjdir (2015). Role of pharmacotherapy in cardiac ion channelopathies. *Pharmacology & Therapeutics* 155 ,132-142.
2. Wikipedia: <https://en.m.wikipedia.org>
3. Isik,Turker, Tomohiko Ai, Hideki Itoh, Minoru Horie (2017). Drug-Induced fatal arrhythmias: Acquired long QT and Brugada syndromes. *Pharmacology & Therapeutics* 176 (48-59).
4. Pieter Postema, Jon Neville, Jonas S.S.G. de Jong, Klaus Romero, Arthur A.M. Wilde, and Raymond L. Woosley (2013). Safe drug use in long QT syndrome and Brugada syndrome: comparison of website statistics. *Europace* 15, 1042-1049.
5. <https://www.crediblemeds.org>
6. <https://www.brugadadrugs.org>