

What is clinically relevant QTc prolongation?

- Normal QTc interval: < 450 ms (men) and < 460 ms (women)
- Some patients may experience arrhythmia (e.g. Torsades de Pointes) with modest QTc prolongation while some patients experience no arrhythmia even at markedly prolonged QTc
- In general, for every 10 ms increase in QTc interval, there is 5-7% increase in risk of an arrhythmia
 - QTc > 500 ms is associated with a substantial increase in risk of Torsades de Pointes

Medication commonly associated with QTc prolongation

Risk Category	Degree of QTc Elevation	Medications
High risk	>20 ms	<ul style="list-style-type: none"> • Antiarrhythmics class Ia and class III • Haloperidol
Potential risk	5 to < 20 ms	<ul style="list-style-type: none"> • <u>Antiemetics</u>: chlorpromazine, droperidol, ondansetron • <u>CNS acting agents</u>: citalopram, escitalopram, tricyclics, paliperidone, ziprasidone • <u>Antifungals/Antibiotics</u>: fluconazole, voriconazole, moxifloxacin • <u>Others</u>: hydroxyzine, methadone, ranolazine, sildenafil
Uncertain risk	< 5 ms	<ul style="list-style-type: none"> • <u>CNS acting agents</u>: atomoxetine, trazodone, venlafaxine, clozapine, olanzapine, quetiapine, risperidone, lithium • <u>Antibiotics</u>: azitromycin, clarithromycin, erythromycin, ciprofloxacin, levofloxacin • <u>Others</u>: chloroquine, clofazimine, rilpivirine, tacrolimus, tizanidine

List is not all-inclusive. For more information visit: <https://crediblemeds.org/healthcare-providers>

Outpatient management of drug-induced QTc prolongation:

When prescribing drugs associated with QTc prolongation:

1. Does the patient have risk factors for QTc prolongation?
 - **Modifiable**: bradycardia, uncorrected electrolyte disturbances (hypokalemia, hypomagnesemia, hypocalcemia), untreated hypothyroidism, recent cardioversion with QTc-prolonging drug
 - **Non-modifiable**: female, age > 65 years, structural heart disease, impaired hepatic or renal function, congenital long QT syndrome
2. Is the new medication associated with a risk of QTc prolongation?
3. Are there drug interactions that could increase the risk of QTc prolongation? (e.g. additive effect, impaired clearance, or electrolyte imbalance)
4. Assess risk vs. benefit of the medication (i.e. is the medication essential)? Are there alternatives?

If the medication is necessary, consider the steps below:

1. Correct modifiable risk factors as much as possible (keep potassium closer to the higher end of normal)
2. Discontinue unnecessary medications, specifically those with known QTc prolongation risk
3. Start the new medication at low dose and titrate up as appropriate. Monitor based on patient's risk factors and medication risk for QTc prolongation:

Drug with **LOW** QTc prolongation risk, **NO** patient risk factors, and **NO** drug-interactions:

No monitoring required unless specified by manufacturer

Drug with **LOW** QTc prolongation risk, in presence of patient risk factors and/or drug-interactions:

Monitor baseline ECG and repeat once drug reaches steady state

Drug with **HIGH** QTc prolongation risk, **NO** patient risk factors, and **NO** drug-interactions:

Monitor baseline ECG and repeat once drug reaches steady state. No regular ECG monitoring needed if patient is asymptomatic

Drug with **HIGH** QTc prolongation risk, in presence of patient risk factors and/or drug-interactions:

Monitor baseline ECG and repeat once drug reaches steady state. Regular ECG monitoring as needed (e.g. high-risk patients, suspected symptoms).

Avoid agents with high QTc prolongation risk in patients with pre-existing QT prolongation. In patients with long QT syndrome, use alternative agents

4. Educate patients on common symptoms of cardiac arrhythmias (lightheadedness or dizziness, palpitation, syncope) and advise when to seek medical attention
5. Consider additional ECG monitoring following dose changes and if patient presents with symptoms while taking medications known to increase risk of QTc prolongation, regardless of patient's risk factors
6. Monitor ECG in cases of significant change in QTc (increase of > 50 ms or absolute value > 500 ms). Check and correct any electrolyte imbalances; if QTc prolongation does not resolve, consider dose reduction or discontinue the medication