Drug induced QT prolongation
Clinical Guidance for Pharmacists

- QT prolongation is a warning signal to alert for the risk of torsades de pointes (TdP); a serious cardiac arrhythmia that can lead to sudden cardiac death.
- QT prolongation and TdP can be transient, variable and unpredictable.
- The longer the QT interval, the greater the risk of TdP.
- QT interval is often represented as QTc (heart rate corrected QT interval).

### STEP 1: IDENTIFY DRUG(S)

- An individual drug on its own may pose a significant risk of QT prolongation and TdP
- CredibleMeds (crediblemeds.org, FREE registration) categorises drugs that prolong the QT interval as follows:

<table>
<thead>
<tr>
<th>CredibleMeds TdP Risk Category - Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Known</td>
</tr>
<tr>
<td>Possible</td>
</tr>
<tr>
<td>Conditional</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CredibleMeds TdP Risk Category - Congenital Long QT Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avoid ALL QT prolonging drugs and adrenergic drugs</td>
</tr>
</tbody>
</table>

### STEP 2: IDENTIFY PREDISPOSING RISK FACTORS

Drug induced QT prolongation potential alone is generally not enough to cause TdP. Clinically significant drug induced QT prolongation tends to occur in patients with predisposing risk factors.

#### Non-modifiable
- Female
- Age over 65
- Past history of drug induced QT prolongation
- Family history of sudden cardiac death
- Structural heart disease
- Thyroid dysfunction
- Bradycardia
- Renal / hepatic impairment that may increase drug concentrations
- Congenital long QT syndrome

#### Modifiable
- Hypokalaemia, hypomagnesemia, hypocalcaemia
- Pharmacokinetic drug interactions
- Pharmacodynamic drug interactions (eg. concomitant use of QT prolonging drugs)
- Drugs causing electrolyte abnormalities (eg. thiazides) or bradycardia (eg. beta blockers)
- Rapid parenteral administration
- High therapeutic doses and overdose

### Prolonged QTc Values by Gender (milliseconds, ms)

<table>
<thead>
<tr>
<th>Gender</th>
<th>QTc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>&gt; 450 ms</td>
</tr>
<tr>
<td>Women</td>
<td>&gt; 470 ms</td>
</tr>
</tbody>
</table>

Greatest risk of TdP and sudden cardiac death:
- QTc > 500 ms
- Greater than 60 ms change from baseline
### STEP 3: MANAGEMENT AND MONITORING

**How can I prevent drug induced QT prolongation/TdP?**
- Consider QT prolongation risk category of drug(s)
- Screen patients for predisposing risk factors
- Consider alternative drugs without QT prolongation risk
- Correct modifiable risk factors
- Use lowest effective dose
- Ensure slowest possible rate of IV administration
- Avoid drug interactions
- Avoid QT prolonging drugs in patients with congenital long QT syndrome

**Who should be monitored for QT prolongation/TdP?**
- Monitoring is most important for patients at greatest risk of TdP
- For example, patients with risk factors and prescribed:
  - at least one drug from known risk of TdP category
  - two or more drugs from any CredibleMeds risk category

**When do I monitor patients if a QT prolonging drug must be used?**
- Baseline electrocardiogram (ECG)
- Repeat ECG once drug steady state reached (3 – 5 half lives)
- Frequency of repeat ECG depends on:
  - duration of therapy
  - dose increase
  - change in patient risk factors
  - detection of QT prolongation

**How do I manage drug induced QT prolongation?**

<table>
<thead>
<tr>
<th>QTc (Males): 450 - 500 ms</th>
<th>QTc (Female): 470 - 500 ms AND/ OR Patient symptomatric (light-headedness, dizziness, palpitations, shortness of breath or fainting)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cease implicated drug(s) where possible If drug treatment necessary:</td>
<td>continue ECG monitoring regularly and with dose changes consider cardiology advice</td>
</tr>
<tr>
<td>- consider dose reduction or select an alternative with lower risk of QT prolongation</td>
<td></td>
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<tr>
<td>Common drugs known to cause TdP:</td>
<td></td>
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<tr>
<td>List is not exhaustive.</td>
<td></td>
</tr>
<tr>
<td>Macrolides</td>
<td>azithromycin, clarithromycin, erythromycin, roxithromycin</td>
</tr>
<tr>
<td>Quinolones</td>
<td>ciprofloxacin, moxifloxacin</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>citalopram, escitalopram</td>
</tr>
<tr>
<td>Anticholinesterases</td>
<td>donepezil</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>haloperidol</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>amiodarone, flecainide, sotalol</td>
</tr>
<tr>
<td>Antifungals</td>
<td>fluconazole</td>
</tr>
<tr>
<td>Immunomodulators</td>
<td>hydroxychloroquine</td>
</tr>
<tr>
<td>Opioids</td>
<td>methadone</td>
</tr>
</tbody>
</table>

For more information

SA Pharmacy Medicines Information Service
Women’s and Children’s Hospital
Phone: (08) 8161 7555 (9am – 5pm Weekdays)
Email: medinfo@sa.gov.au

Suggested resources:
- [CredibleMeds](http://www.crediblemeds.org)
- [Stockley’s Drug Interactions](http://www.stockleys.com)

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