Guidelines for the Management of QTc Prolongation with Psychotropic Medication

NHS Tees, Esk and Wear Valleys NHS Foundation Trust

Quick reference guide and links to contents: *(accessible version available on request)*

- Prescribing decision support algorithm
- What is the QT interval, how to measure it & adjust for heart rate
- Reference ranges for prolonged QTc interval (men QTc >440 msec, women QTc >470 msec) & age-related differences (children/older adults)
- Patient and drug-specific risk factors for Torsade de Pointes to enable completion of following risk assessment when initiating new medication:
  - Does the **patient** have any risk factors for QT prolongation?
  - Is the **new medication** associated with a risk of QT prolongation?
  - Are there any **potential drug interactions** that could increase the risk of QT prolongation?
  - Is the medication **essential**? Are there any alternatives?
- When to conduct an ECG, what to do if ECG identifies abnormal QTc interval & when to refer to cardiology

Patient-specific risk factors (see page 4)

- Electrolyte disorders
- Drugs/conditions which may impact on electrolytes
- Kidney or liver disease
- Age ≥ 65 years
- Female gender
- Baseline QTc interval >480 msec
- Personal history/congenital or family history of long QT syndrome
- Cardiac risk factors
- Untreated thyroid disease
- Unexplained syncope/presyncope
- Family history of sudden cardiac death or syncope
- Prescribed a drug that may affect elimination of the psychotropic drug, e.g. affecting cytochromes or drug transporters required for elimination
- Drug toxicity, e.g. due to patient's metaboliser status, drug interaction or accidental or intentional overdose
- Prescribed another drug with potential to prolong QTc interval
- Methadone dose ≥100 mg/day

More information on QT-prolongation potential of drugs & interactions:
BNF; www.crediblemeds.org;
Manufacturer SPC's www.medicines.org.uk

Psychotropic Drugs with potential effects on QTc interval (see table 2 for more detail)

Low effect Only in overdose or average increase **<10 msec**		**Moderate effect** Average increase of **10-20 msec** at therapeutic doses	**High effect** Significant average increase at therapeutic doses **usually >20 msec**
Amitriptyline Aripiprazole Buprenorphine Bupropion Clozapine Donepezil Duloxetine Fluoxetine Flupentixol Fluphenazine Galantamine Lithium Lofepramine	Memantine Mirtazapine Olanzapine Paliperidone Perphenazine Prochlorperazine Promethazine Risperidone Rivastigmine Sulpiride Trazodone Venlafaxine Zuclopenthixol	Amisulpride Chlorpromazine Citalopram Clomipramine Escitalopram Haloperidol Imipramine Levomepromazine Methadone (esp. doses >100mg) Nortriptyline Quetiapine Trimipramine	Any IV antipsychotic *Pimozide* *Sertindole* *Thioridazine* Any drug or combination of drugs used in doses exceeding recommended maximum (HDAT)

Non-psychotropic Drugs with potential to prolong QTc interval (not exhaustive – see table 1)

Anti-arrhythmics	Amiodarone, Disopyramide, Dronedarone, Flecainide, Procainamide, Quinidine, Sotalol
Antibiotics & anti-fungals	Azithromycin, Ampicillin, Ciprofloxacin, Clarithromycin, Co-trimoxazole, Erythromycin, Fluconazole, Ketoconazole, Levofloxacin, Moxifloxacin, Ofloxacin
Anti-emetics	Droperidol, Domperidone, Ondansetron
Others	Amantadine, Anagrelide, Bendroflumethiazide and loop diuretics, Chloroquine, Cilostazol, Ciclosporin, Diphenhydramine, Hydroxyzine, Mefloquine, Nicardipine, Pentamidine, Quinine, Tacrolimus, Tamoxifen, Vandetanib

Title	Guidelines for the Management of QTc Prolongation with Psychotropic Medication		
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Prescribing decision support algorithm – prescribing drugs with potential to prolong QTc interval *(accessible version available on request)*

Need for new psychotropic drug identified

Evaluate patient TdP risk (including risk factors related to current medication) and correct any modifiable risk factors e.g., electrolyte imbalance

LOW RISK PATIENT & no concurrent QT prolonging medication

Check risk stratification of preferred psychotropic drug (Table 2 or other resource e.g., Crediblemeds)

LOW / MODERATE RISK DRUG

- Usual follow up, no additional monitoring necessary unless specified by manufacturer or symptomatic

HIGH RISK DRUG

- Baseline ECG
- Early follow up & ECG 1-3 weeks after dose change
- Check for any new symptoms/concerns on ECG
- Repeat ECG once drug at steady state.
- Ongoing monitoring not recommended if asymptomatic, unless required by manufacturer

HIGH RISK PATIENT &/or Concurrent QT prolonging medication

(Seek alternative drugs for patients with congenital long QT syndrome)

Check risk stratification of preferred psychotropic drug & for any potential contraindicated combinations (Table 2 or other resource e.g., Crediblemeds)

LOW RISK DRUG

- **If concurrent QT prolonging drug:** Baseline ECG recommended; repeat once new drug at steady state.
- **Otherwise:** usual follow up, no additional monitoring necessary unless specified by manufacturer or symptomatic

MODERATE RISK DRUG

- Baseline ECG
- Early follow up & ECG 1-3 weeks after dose change
- Check for any new symptoms/concerns on ECG
- Repeat ECG once new drug at steady state.
- Ongoing monitoring not recommended if asymptomatic, unless required by manufacturer (e.g., es/citalopram 6-monthly)

HIGH RISK DRUG

Avoid in patients with existing QTc prolongation

- Baseline ECG & cardiology input recommended prior to prescribing

Only if cardiology & analysis of risk/benefits supports prescribing:

- Early follow up & ECG 1-3 weeks after dose change
- Check for any new symptoms/concerns on ECG
- Repeat ECG once new drug at steady state, then regular ECG monitoring

ACTION

- All patients who present with palpitations, light headedness, or dizziness while prescribed a medication with the potential to prolong the QTc interval should be offered an ECG regardless of other risk factors. Cardiology follow up should be sought where appropriate (e.g., history suggestive of arrhythmia, prior cardiac event).
- Additional ECG monitoring should be considered with any dose increase or the addition of a new risk factor e.g., drug interaction, concomitant use of another potential QTc-prolonging drug, etc.
- If ECG identifies abnormal **QTc <500 msec**, consider reducing dose/switching to alternative lower risk drug, address any non-pharmacological modifiable risk factors, repeat ECG in 1-2 weeks and consider referral to cardiology (Immediate referral if associated with unexplained CV symptoms or unable to alter current potential QTc-prolonging drug).
- If ECG identifies marked QTc interval prolongation (**>500 msec**), or a sudden increase of QTc interval (**>60 msec** from baseline), refer to cardiology urgently, stop the suspected causative agent and switch to lower risk alternative, address any non-pharmacological modifiable risk factors and repeat ECG in 1-2 weeks or sooner. If syncope/presyncope are also present, this an emergency which requires immediate referral for continuous ECG monitoring.

Background

Many drug therapies are associated with prolongation of the QT interval. This is an independent risk factor for developing Torsades de Pointes (TdP), a potentially life-threatening cardiac arrhythmia, and sudden cardiac-related death.

Most case reports of TdP associated with psychotropic drugs include additional risk factors such as:

- Patient-specific factors e.g., advanced age, female sex, hypokalaemia, hypomagnesaemia, bradycardia, and/or heart disease.
- Factors increasing drug exposure e.g., drug overdose or impaired drug elimination due to a drug interaction.

And/or:

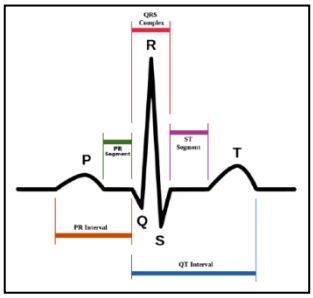
- Concomitant administration of another drug known to prolong the QT interval.

It is therefore important to consider drug-related and individual patient factors prior to prescribing any new psychotropic drugs.

QT prolongation might worsen weeks, months, or years after treatment is started because of changes like the addition of potentially interacting drugs or the appearance of new medical conditions that cause electrolyte imbalances (particularly hypokalaemia and/or hypomagnesaemia), otherwise affect the QT interval, or increase the plasma concentrations of psychoactive drugs.

The QT interval

The QT interval measures the time between the start of ventricular depolarisation and the end of ventricular repolarisation, represented on an ECG by the beginning of the Q wave to the end of the T wave. There is variation in QT intervals between ECG leads, lead II is usually the basis of most reference ranges.



To minimise inconsistencies, it is best to measure the tangent of the descending T wave to baseline in leads II or V5. The tangent of the downslope of the T wave is taken to the baseline of the ECG and the QT interval measured in seconds between the Q wave and point where the tangent hits the baseline. It is important to use seconds as the measurement rather than milliseconds in the calculation if using a calculator or the QTc value will be incorrect. An average of 3–5 beats should be measured.

QT interval varies dependent on the length of the cardiac cycle and is usually corrected (QTc) for heart rate, several formulas can be used for this, most commonly Bazett's formula is used ($QTc=QT/\sqrt{RR}$; QT interval in seconds, RR cardiac cycle in seconds), other correction formulae such as Frederica, Hodges or Framingham may be used. Correction of QT interval for heart rate is controversial and inexact. The reliability of the standard QTc decreases at higher heart rates.

The major limitation of Bazett's formula is that it overestimates QTc interval at any heart rate much higher than 60 beats per minute (bpm) and underestimates QTc interval at rates lower than 60 bpm. It is therefore recommended to use the Frederica formula if heart rate < 60bpm or >100bpm.

Definitions for QT prolongation vary in the literature, but for **men QTc >440 msec** and for **women QTc >470 msec** are commonly used. The risk of TdP increases with increasing QTc, for every 10 msec increase, there is a ~5-7% increase in the risk of arrhythmic events. When QTc is greater than 500 msec for both men and women and/or an increase of >60 msec from baseline, risks are higher, and urgent action is required.

Stress/anxiety can affect an ECG & it may be necessary to manage the patient's anxiety and repeat the ECG if affected.

Pregnancy

A systematic review and meta-analysis of 57 studies revealed a significant QTc interval lengthening that increases throughout subsequent trimesters of normal pregnancy, with a 10 msec average increase during the first trimester and 20 msec increase during the second and third trimesters compared with nonpregnant individuals. Preeclampsia further significantly augmented this increase during the third trimester by an additional 20 msec average increase compared with the normal third-trimester pregnancy.

QTc prolongation is more prevalent and QTc intervals are significantly longer in twin pregnancies as compared to single pregnancies.

Please seek advice from perinatal team if considering psychotropic medication in pregnancy.

Age-related differences in QTc values

Children and older people may be more susceptible to QT changes.

Children and Young People

Some literature sources state that there is an absence of gender difference until early adolescence and suggest a normal QTc (Bazett's formula) of <440 msec age 1-15 years, with QTc values >460 msec considered prolonged in this age group. At age 16 and over, they suggest that adult reference ranges (see above) should be used.

Other literature sources suggest that in young people aged between 13 and 16, gender does influence QT interval, in some studies longer QTc intervals were observed in girls over 14 years old compared with boys. It is thought that this is due to QT shortening after puberty in boys rather than QT lengthening in girls.

Heart rate and the effect of heart rate on the performance of QT correction factors is more variable in the paediatric age range, it is therefore suggested that the threshold for seeking specialist cardiology advice may be lower in paediatric patients than in adult patients.

Older adults (over 65 years old)

It should be noted that the predisposition to prolonged QT interval in women diminishes with increasing age, it has been suggested that cardiac ion channel activity is altered by sex hormones, which in turn affects the QT interval. Differences in cut-off points between men and women are therefore not as relevant among older people.

TdP Risk Factors

Before prescribing a new psychotropic drug for a patient, prescribers should take into consideration patient-specific risk factors and the risk-rating of the proposed drug, these must then be balanced against the benefits of treatment with the proposed drug. (See algorithm)

Prescribers should also consider whether there are any alternative solutions that could reduce the risk of QT prolongation without compromising overall safety and efficacy.

The following approach to risk-assessment is recommended:

1. Does the **patient** have any risk factors for QT prolongation?
2. Is the **new medication** associated with a risk of QT prolongation?
3. Are there any **potential drug interactions** that could increase the risk of QT prolongation?
4. Is the medication **essential**? Are there any alternatives?

Electrolyte imbalances may need correcting prior to prescribing a new drug with potential to prolong the QTc interval and patients should be warned to avoid other QTc prolonging medications (prescribed and those available to buy over the counter e.g., diphenhydramine).

Combinations of risk factors have been shown to correlate with subsequent prolongation of the QTc interval in at-risk patients and potential cumulative effects must be seriously considered.

For a low TdP risk patient – choose the drug with best psychiatric benefit/risk ratio for their condition, for a patient with higher TdP risk e.g., multiple risk factors, evaluate the cardiac risk and psychiatric efficacy of available agents prior to selecting a drug to prescribe (See table 2). Higher risk drugs should be avoided in patients with existing QTc prolongation.

As part of shared decision making, for patients with an elevated risk of TdP, the decision to commence a QT-prolonging drug should be made collaboratively with the patient, and the potential impact should be clearly communicated. Patients should be educated on the common symptoms of cardiac arrhythmias—such as dizziness, palpitations and syncope—and advised on when to seek medical attention. Choice and medication offer a handy fact sheet "Prolonged QT interval from medicines" to support TEWV staff with these discussions. The discussion, information provision and decision to initiate treatment (or not) should be recorded in the electronic patient record.

Patient-specific risk factors

(A comprehensive list of potential patient-specific risk factors is available at www.crediblemeds.org; the risk factors with the most significant impact are highlighted in bold)

Most clinical cases of drug-induced QT prolongation occur in the presence of at least one of these risk factors, and >70% occur in the presence of two or more.

- Electrolyte disorders – hypokalaemia, hypomagnesaemia, hypocalcaemia, risk increases with **lower levels**. (Hypokalaemia-related QTc prolongation is commonly observed in acute psychotic admissions)

- Drugs or conditions which may impact on electrolytes e.g., diuretics, dietary supplements, severe acute illness, gastroenteritis, endocrinopathies, eating disorders (purging behaviours and dietary restriction), starvation, binge drinking in alcohol use disorder, extreme physical exertion, fasting behaviours,
- Kidney or liver disease (**risk increases with increased severity**) – also consider impact on metabolism of other drugs/risk of increased adverse effects
- Age ≥ 65 years
- Female sex
- **Baseline QTc interval >480 msec**
- **Personal history/congenital or family history of long QT syndrome**
- **Cardiac risk factors such as heart failure, left ventricular hypertrophy, bradycardia (heart rate <60), IHD, myocarditis, MI**
- Untreated thyroid disease – more common with hypothyroidism
- **Unexplained syncope/presyncope**
- **Family history of sudden cardiac death or syncope**
- Prescribed a drug that may affect elimination of psychotropic drug e.g., affecting cytochromes or drug transporters required for elimination
- Drug toxicity e.g., due to patient's metaboliser status, drug interaction or accidental or intentional overdose
- **Prescribed another drug with potential to prolong QTc interval**
- **Methadone dose ≥100 mg/day**

Drug-specific risk factors

Information on the potential of an individual drug to prolong the QTc interval is available from various sources which may offer slightly different risk stratification/risk categories. Data are often inconclusive about arrhythmic risk for drugs that increase the QTc interval by <20 msec; drugs associated with a change in baseline QTc of >20 msec are of greatest concern and are generally categorised as higher risk regardless of source used.

Some drugs may cause adverse effects that may increase the potential for QTc interval prolongation, but this may not flag routinely on all interaction checkers, for example ivabradine can cause bradycardia and should be avoided in patients taking other QT prolonging drugs.

Reliable sources for information on QT prolongation include:

- Crediblemeds website (https://www.crediblemeds.org/) or download mobile phone app (US-based resource, doesn't include all UK licensed drugs; there is now a subscription charge for app)
- Maudsley – Prescribing (access online with Athens password) and Physical Health guidelines (paper copy)
- Psychotropic Drug Directory (UK resource available via Medicines Complete subscription only, access via pharmacy team)
- Stockley's Drug Interactions (UK resource, available via Medicines Complete subscription only, access via pharmacy team)
- Manufacturer information - Summary of Product Characteristics (UK resources, search by drug, "Electronic Medicines Compendium" (EMC) www.medicines.org.uk or "MHRA Products page" https://products.mhra.gov.uk/)

Some of the more common non-psychotropic drugs that can cause QT-prolongation are listed in table 1; table 2 lists the potential impact of psychotropic drugs on the QTc interval.

In the UK, the MHRA has issued safety alerts regarding the QT prolonging potential of specific drugs including es/citalopram, domperidone, ondansetron, quinine and tamoxifen. There are some psychotropic drugs where the manufacturer specifically contra-indicates use with other drugs with potential to prolong the QT-interval.

For example, the manufacturer of citalopram contra-indicates its use with other medicinal products that are known to prolong the QT-interval e.g., Class IA and III antiarrhythmics, **antipsychotics** (e.g., phenothiazine derivatives, pimozide, haloperidol), **tricyclic antidepressants**, certain antimicrobial agents (e.g., sparfloxacin, moxifloxacin, erythromycin, pentamidine, anti-malarial treatment particularly halofantrine), certain antihistamines (astemizole, mizolastine).

Es/Citalopram Safety Advice

In December 2011 (updated in December 2014), the MHRA issued the following advice due to the risk of dose-dependent QT prolongation with these drugs:

- **Citalopram** - maximum dose 40 mg/day in adults, and 20 mg/day in adults over 65 years and adults with hepatic impairment/poor metabolisers (CYP2C19).
- **Escitalopram** – max. dose 20 mg/day in adults, and 10 mg/day in adults over 65 years and adults with hepatic impairment/poor metabolisers (CYP2C19).
- Both drugs are **contra-indicated** in patients with known QT prolongation, congenital long QT syndrome or taking other QT-prolonging medication, (see also advice on prescribing contra-indicated combinations).
- Both drugs are **cautioned** in patients with risk factors for QT prolongation, e.g. recent MI, particularly at higher doses.

All patients identified on doses above the licensed maximum for their age group/metaboliser status should be reviewed and the most appropriate action taken, options include:

- Complete a gradual, stepwise dose reduction to the maximum licensed dose and monitor for efficacy for three months following dose reduction, if the patient remains stable, continue with the licensed dose.
- Switch to an appropriate licensed alternative antidepressant for the indication (see SPS switching guide for switching advice), monitoring for efficacy, any withdrawal symptoms or signs of serotonin syndrome.
- If identified as needing to continue at greater than the maximum licensed dose, i.e. due to past history, prescribed indication or if all other options have been exhausted, consider maintaining the previously effective dose:
  - Document unlicensed dose, rationale and evidence of informed consent (from patient with capacity) in electronic patient record.
  - Reduce and monitor any other risk factors for QTc prolongation.
  - Monitor with regular ECG (e.g. initially, 6-monthly and after any medication or dose changes).
  - Advise patient to report any abnormal heart rate or rhythm.
  - If significant QT prolongation detected, seek specialist advice and/or switch.

Another example is that the manufacturer of chlorpromazine, specifically contra-indicates its use with es/citalopram.

Prior to prescribing a new medication, **all** current physical health and psychotropic medication should be checked against a reliable source for their QT-prolongation potential.

It is important to recognise that the extent and the associated risk of developing QT prolongation when combining drugs with QT-prolonging effects are still unknown, but such combinations do not necessarily have an additive effect, and a pragmatic approach should be taken which considers both patient and drug specific risk factors.

However, a recent study has demonstrated that low-dose adjunctive aripiprazole (up to 5 mg/day) did not prolong QTc interval in patients stabilised on either olanzapine, risperidone or clozapine.

Whilst it is not recommended as standard practice, it is recognised that on occasion, combinations that are contra-indicated by the manufacturer, may be considered clinically appropriate after exhausting all other potential options (e.g., citalopram + antipsychotic; haloperidol for RT when other QT-prolonging drugs are being taken regularly).

In these circumstances, prescribing such a combination would be outside of the product licence and appropriate steps should be taken to identify and manage potential risks prior to prescribing. The patient should be informed of the planned off-label prescribing, (there are choice and medication leaflets available to support these discussions), their consent should be obtained and documented.

Table 1: Non-psychotropic Medication known to prolong QTc-interval
(this list is not exhaustive)

Drug Group	Drugs	
Anti-arrhythmics	Amiodarone Disopyramide Dronedarone Flecainide	Procainamide Quinidine Sotalol
Antibiotics	Azithromycin Ampicillin Ciprofloxacin Clarithromycin Co-trimoxazole	Erythromycin Levofloxacin Moxifloxacin Ofloxacin
Anti-emetics	Droperidol Domperidone Ondansetron	
Anti-fungals	Fluconazole Ketoconazole	
Others	Amantadine Anagrelide Bendroflumethiazide and loop diuretics (hypokalaemia) Chloroquine Ciclosporin Cilostazol Diphenhydramine	Hydroxyzine Mefloquine Nicardipine Pentamidine Quinine Tacrolimus Tamoxifen Vandetanib

Note: β2 agonists and sympathomimetics may provoke TdP in patients with prolonged QTc.

Table 2: Psychotropic Medication – by potential impact on QTc-interval *(a more accessible version of this table is available on request)*

Drug Group / Drugs		Impact on QTc Interval				
		Unknown	**No known effect** (At therapeutic dose/in overdose)	**Low effect** Only in overdose or average increase **<10 msec**	**Moderate effect** Average increase of **10-20 msec** at therapeutic doses	**High effect** Significant average increase at therapeutic doses **usually >20 msec**
	Antipsychotics	Loxapine Pipotiazine Trifluoperazine	Brexpiprazole Cariprazine Lurasidone	Aripiprazole Clozapine Flupentixol Fluphenazine Olanzapine Paliperidone Perphenazine Prochlorperazine Risperidone Sulpiride Zuclopenthixol	Amisulpride *Chlorpromazine* *Haloperidol* *Levomepromazine* Quetiapine	Any IV antipsychotic *Pimozide* *Sertindole* *Thioridazine* Any drug or combination of drugs used in doses exceeding recommended maximum (HDAT)
	Anti-depressants[1]		Agomelatine Esketamine Paroxetine[2] Fluvoxamine[2] Sertraline[2] Reboxetine Vortioxetine	*Fluoxetine*[2] Venlafaxine Bupropion Duloxetine Lofepramine Mirtazapine Amitriptyline[3] Trazodone	*Citalopram*[6] *Escitalopram*[6] *Clomipramine*[3] Trimipramine[3] Nortriptyline[3] *Imipramine*[3]	
	Others	Buspirone	Methylphenidate Atomoxetine Lis/dexamfetamine Guanfacine Clonidine Melatonin Topiramate Carbamazepine Valproate Lamotrigine Benzodiazepines Gabapentin Pregabalin Daridorexant	Buprenorphine *Lithium*[4] Promethazine Memantine Galantamine[5] Donepezil[5] Rivastigmine[5]	*Methadone* especially doses >100mg	

1. Information not included for MAOIs, please see individual product information prior to prescribing.
2. Cytochrome P450 inhibitor, may prolong QTc interval if prescribed in combination with another QTc prolonging drug.
3. Risk is increased at doses ≥100mg/day amitriptyline equivalent.
4. Some sources suggest that lithium may produce a greater increase in QTc interval during initiation (average 19 msec), with high serum levels or with concurrent electrolyte imbalances.
5. There is conflicting information about the QTc prolongation risk with AChEIs, they have been included in the lower risk category but should be used with caution in patients with other risk factors for QTc prolongation e.g. bradycardia, prescribed other QTc prolonging drugs etc. Prescribers should consider an ECG.
6. Risk is increased at doses above licensed maximum: citalopram 40mg/day (20mg/day age ≥ 65 years); escitalopram 20mg/day (10mg/day age ≥ 65 years). 6 monthly ECG monitoring recommended for patients prescribed doses > licensed maximum.

Drugs where an ECG is recommended by manufacturer in certain circumstances (see when to obtain ECG for details) are listed in ***italics***.

When to obtain an ECG

Due to the wide variety of physiologic and pharmacologic factors that can influence the QTc interval; it is recommended that QTc interval measurement should be no more than one month prior to the prescribing decision point, and no substantial changes in medications, electrolytes, or cardiovascular status (e.g., an episode of heart failure or an acute MI) should have occurred after the measurement. If there is uncertainty regarding the patient's status, an ECG should be considered. Most patients will have no symptoms, even if their QT interval is prolonged.

Clinicians should consult Trust guidelines surrounding the baseline and ongoing ECG monitoring for specific medications e.g., Trust psychotropic drug monitoring guidance, the following is a summary of when an ECG is recommended:

- If a physical examination has identified a specific cardiovascular risk (such as hypertension or irregular pulse).
- If admitted as an in-patient.
- If there is a family history of cardiovascular disease, a history of sudden collapse, or other cardiovascular risk factors such as cardiac arrhythmia.
- If a pre-treatment ECG is recommended by the manufacturer e.g.,
    - Es/citalopram, fluoxetine, clomipramine in patients with stable cardiac disease
    - Imipramine – monitoring of cardiac function recommended in elderly patients
    - Antipsychotics such as chlorpromazine, haloperidol, levomepromazine, pimozide, sertindole and thioridazine.
    - Lithium in patients with cardiovascular disease/risk factors.
    - ADHD medication in patients with potential cardiovascular risk factors
    - Methadone
        - ECG monitoring is recommended prior to methadone treatment, with a further ECG at dose stabilisation in patients with recognised risk factors of QT prolongation, or in case of concomitant treatment with drugs that have a potential for QT prolongation.
        - ECG monitoring is recommended in patients without recognised risk factors for QT prolongation, before dose titration above 100 mg/day, and at seven days after titration.
- If patient is already taking certain medicines which are known to cause ECG abnormalities (e.g., erythromycin, fluconazole, domperidone, anti-arrhythmics)
- If the patient is on high dose antipsychotic therapy (HDAT)
- If the patient has factors which may predispose to arrhythmias (see patient-specific factors) including e.g.,
    - Electrolyte abnormalities – hypokalaemia, hypocalcaemia, hypomagnesaemia.

  - Systemic disease – liver disease, renal disease, hypothyroidism.

- The date any ECG is completed and any relevant findings including QTc interval should be documented in the appropriate section of the patient's electronic record as well as filing the ECG within their paper notes/scanning onto the patient's electronic record.
- Where a baseline ECG is recommended above, this should be repeated at least annually unless otherwise specified.
- Additional ECG monitoring should be considered with any dose increase or the addition of a risk factor e.g., drug interaction, concomitant use of a QTc-prolonging drug, etc.
- All patients who present with palpitations, light headedness, or dizziness whilst prescribed a medication with the potential to prolong the QTc interval should be offered an ECG regardless of other risk factors. Cardiology follow up should be sought where appropriate (e.g., history suggestive of arrythmia, prior cardiac event).
- If ECG identifies abnormal QTc **<500 msec**, consider reducing dose or switching to alternative lower risk drug, address any non-pharmacological modifiable risk factors, repeat ECG in 1-2 weeks and consider referral to cardiology (Immediate referral if associated with unexplained CV symptoms or unable to alter current potential QTc- prolonging drug).
- If ECG identifies marked QTc interval prolongation (**>500 msec**), or a sudden increase of QTc interval (**>60 msec from baseline**), refer to cardiology urgently, stop the suspected causative agent, and switch to lower risk alternative, address any non-pharmacological modifiable risk factors, repeat ECG in 1-2 weeks or sooner. If syncope/presyncope are also present, this an emergency which requires immediate referral for continuous ECG monitoring.

When to use the AliveCor KardiaMobile 6 lead ECG device (NICE guidance, 2023)

The KardiaMobile 6L allows ECG recording with no need for undressing and without using conductive stickers or gel. KardiaMobile 6L ECG can be recorded during a routine home visit by a community health professional. This may reduce stress and anxiety. KardiaMobile 6L is not intended for use in children and should not be used in patients where a potential risk of them swallowing the device has been identified. (not licensed for use in under 18's)

KardiaMobile 6L can be used in psychiatric services in all patients over 18 years of age as an option to measure cardiac QT interval both before initiation or for monitoring of **antipsychotic medication** while more evidence is generated only if:

- A repeat QT interval measurement using a 12-lead electrocardiogram (ECG) device is offered to:
  - women with a corrected QT interval (QTc) longer than 470 milliseconds
  - men, trans people having hormone treatment, and intersex people who have QTc longer than 440 milliseconds
  - people who have a follow-up ECG with more than a 50-millisecond increase in QTc.

For trans people not having hormone treatment, use the QTc threshold for their sex registered at birth.

- Training for healthcare professionals on recording an ECG and measuring and interpreting QT interval is provided. Trust training is available via this link

- People are offered information about why this testing is done and why testing may be repeated using a 12-lead device after it has been measured using KardiaMobile 6L.

This ECG device is currently only used for QT measurement and not for detecting any other cardiac problem. Please use 12 lead ECG for cardiac emergency or escalate using your local clinical policy and practice.

The following online calculators are recommended to calculate the QTc interval (using the appropriate formula as described earlier in this document) from the ECG generated by the device:
https://www.mdcalc.com/corrected-qt-interval-qtc
Mayo Clinic corrected QT interval (QTc) calculator - Medical Professionals

When to consult cardiology

Routine cardiology consultation is not indicated when prescribing QTc interval prolonging medications to a patient without cardiac risk factors; however, many higher risk clinical scenarios are best approached with cardiology input.

In patients with known heart disease and one or more risk factors for drug induced TdP, the clinician may consider consulting with the existing cardiologist when starting a medication with liability. In higher risk scenarios including co-administration of high-risk medications (e.g., amiodarone and parenteral haloperidol), marked QTc interval prolongation (>500 msec), or a sudden increase of QTc interval (>60 msec from baseline), referral to cardiology is appropriate.

Patients on a known offending drug who experience cardiac symptoms such as syncope, dizziness, and palpitations should immediately be referred to cardiology.

For specialist cardiology advice contact your local on-call cardiologist. It is recommended that you have the following information collated prior to seeking advice and are able to share a copy of the relevant ECG(s) with the cardiologist:

1. What medications have been prescribed for the patient's mental health condition?
2. What other medications is the patient taking (comprehensive list)?
3. Has the patient experienced any faintness, near collapse or collapse episodes?
4. Is the patient known to have any cardiac history / conditions?
5. What was the patient's heart rate and QTc (rate corrected QT-interval from the automatic report at the top of the tracing) before starting therapy?
6. What is the patient's latest heart rate and QTc measurement?
7. Biochemistry results (within last two weeks): sodium, potassium, urea, creatinine, eGFR [+ magnesium level if potassium (< 3.5mm/L]; FBC results
8. Do you have alternative medication options open to you if the current regime needs to be changed because of excessive prolongation in the QT-interval?

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