GUIDELINE ON MONITORING PSYCHOTROPIC[1] PRESCRIBING IN RELATION TO CARDIOVASCULAR DISEASE

1. Background

The purpose of this guideline is to provide pragmatic advice to clinicians on lowering the risk of cardiac arrhythmia during treatment with psychotropic medication.

1.1. Cardiac effects of psychotropic medication.

Adverse cardiac outcomes, particularly life threatening arrhythmias (torsade de pointes) and sudden death, are associated with a range of psychiatric medications for psychosis, depression and substance misuse. The main mechanism is prolongation of the QTc interval which is a risk factor for ventricular arrhythmias. Psychotropic medication differs in its propensity to induce QT prolongation, but most effects are dose related.

Drug-induced QTc prolongation is not inevitably related to risk of arrhythmia but arrhythmia is more likely to occur when other risk factors are present, predominantly pre-existing cardiovascular disease.

Clozapine is also associated with cardiomyopathy and myocarditis, particularly in the first few months of treatment. The risk may be as high as 1 in 1000 patients. The ECG may show ST depression but patients should also be monitored for symptoms and signs of heart failure.

Some psychotropic medication increases appetite and weight gain, and can directly cause metabolic syndrome, dyslipidaemia, hypertension and insulin resistance, all of which increase cardiac mortality rates.

1.2. Other drug factors

Many non-psychiatric drugs are associated with QTc prolongation and can exacerbate the effect of psychiatric medication. Examples include antibiotics, anti-arrhythmia and anti-malarial drugs, methadone and tamoxifen.

Drug interactions can also exacerbate impact on QTc, for example, cytochrome p450 inhibitors and inducers, and potassium and magnesium wasting diuretics.

Rapid tranquillisation and use of high dose antipsychotics also increases risk of dangerous arrhythmia.

[1] The term ‘psychotropic’ refers to the full range of prescribed psychiatric medication, including opioids. Staff must be aware that patients may also be taking non prescribed psycho-active substances, which might impact on physical health, and care and prescribing decisions.

1.3. Patient factors

Patients with serious mental illness have a high prevalence of adverse health behaviours; including smoking, low physical activity, poor nutrition and substance misuse. However, the most significant risk factor for anti-psychotic induced sudden death is established or occult cardiovascular disease.

Other key risk factors for serious arrhythmia following psychotropic medication include:

- Long QT syndrome (and family history of LQTS or sudden death[2])
- Bradycardia
- Hypokalaemia, hypomagnesaemia and hypocalcaemia.
- Starvation
- Female gender and age over 70 years.

1.4. Current standards

NICE guidelines advise baseline and follow up ECGs when prescribing anti-psychotic or opioid medication for inpatients or those with cardiovascular risks.

The British Heart Rhythm Society published clinical practice guidelines on the management of patients developing QT prolongation on antipsychotic medication in 2019(1). General principles outlined include:

- Assume all antipsychotics carry an increased risk of sudden cardiac death
- Prescribe the lowest antipsychotic dose possible and avoid polypharmacy/metabolic interactions.
- Perform ECG on admission, before discharge, and at yearly check-up.
- Consider measuring QTc within a week of reaching therapeutic doses of moderate/high-risk antipsychotics.

The SPCs (Summary of Product Characteristics) of psychiatric medications specify when ECGs should be included in medication monitoring. The SPC is a legal document and clinicians would need strong grounds to not comply with this advice.

[2] *Brugada syndrome is an inherited condition affecting the cardiac sodium channel and can lead to syncope or sudden death. Characteristic ECG changes may be present all the time (coved ST elevation in V1 and V2, descending to an inverted T wave resembling RBBB) or may be unmasked by treatment with lithium or TCAs.*

2. Pathway (summarised in Figure 1)

2.1. Assessment

All patients should have an appropriate physical health assessment before being prescribed psychiatric medication, and as part of longer term medication monitoring. Requirements are set out in the Clinical Guideline on Physical Healthcare and the Mental Health Formulary and Prescribing Guidelines.
Baseline ECG is required before prescribing psychotropic medication or if any one of the following risk factors is present:

- The patient has a history, symptoms or signs of established or occult cardiovascular disease;
- If there are independent vulnerability factors (family history, poly- pharmacy, potential drug interactions, disordered electrolytes);
- If a higher risk medication is essential to care (see Table 1).

2.2. Management

Ensure known cardiac disease is under appropriate follow-up: correct modifiable risk or vulnerability factors; review existing medication risks, including poly-pharmacy; and correct abnormal electrolytes.
Abnormalities in the baseline ECG should be discussed with the responsible primary care team and cardiology referral considered for serious ECG abnormalities. These include:

- Prolonged QTc > 500 ms
- Any conduction abnormality apart from RBBB
- Bradycardia < 50 bpm
- ST segment deviation or abnormal T wave morphology
- Pathological Q waves.
- Voltage criteria for Left ventricular hypertrophy

If the QTc is borderline (>440 ms in men or >470 ms in women, but <500 ms), consider reducing the dose or switching to an alternative drug, and consider cardiology review.
Repeat the ECG:

- After steady state medication is reached;
- After a change in medication, a change in dose or poly-pharmacy;
- Change in risk status of the patient;
- At the annual physical health check-up.

Figure 1: Pathway to manage cardiovascular risks associated with psychiatric prescribing

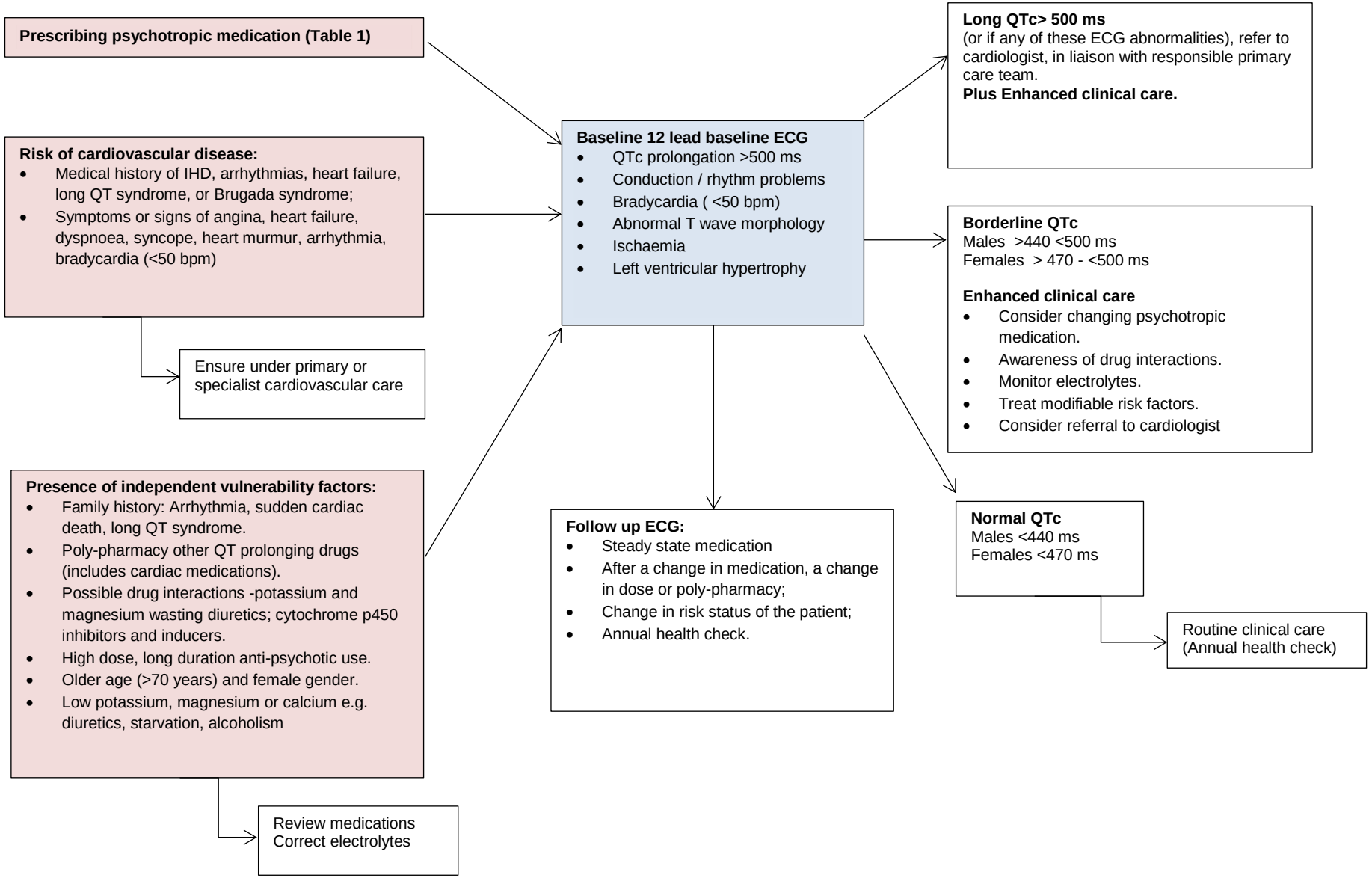

Table 1: Psychotropic medication and risk of cardiac arrhythmia

	SPC **ECG screening recommended** (note 2)	**Maudsley** **Prescribing guidelines** **12th edition** (note 3)
Typical anti-psychotics		
Haloperidol	Yes	Moderate effect
Chlorpromazine	Yes	Moderate effect
Flupentixol	No *	Low effect
Sulpiride	No *	Low effect
Trifluoperazine	No *	Unknown effect
Zuclopenthixol	No	Unknown effect
Fluphenazine decanoate	Yes	Low effect
Carbamazepine	No	No effect
Benperidol	*Yes*	
Levomepromazine	*Yes*	Moderate effect
Pericyazine	*Yes*	
Pimozide	*Yes*	*High effect*
Prochlorperazine	*Yes*	*Low effect*
Promazine hydrochloride	*Yes*	
Atypical antipsychotics		
Risperidone	No	Low effect
Amisulpride	Yes	Moderate effect
Aripiprazole	No	Low effect
Clozapine	Yes	Low effect
Olanzepine	No	Low effect
Quetiapine	No	Moderate effect
Paliperidone	No	Low effect
Mood stabilisers		
Lithium	Yes	Low effect
Asenapine	No	Low effect
Valproate	No	No effect
Lamotrigine	No *	No effect
Approved drugs for depression in adults		
TCA		
Amitriptyline	Yes	Moderate effect
Nortryptyline	*Yes*	*Moderate effect*
Imipramine	No *	Moderate effect
Lofepramine	No	Moderate effect
Trazodone	No *	Low effect
MAOI		
Phenelzine	No	No effect
Moclobemide	No	Low effect

	SPC **ECG screening recommended** (note 2)	**Maudsley** **Prescribing guidelines 12th edition** (note 3)
Clomipramine	Yes	No effect
SSRI		
Sertraline	No *****	No effect
Paroxetine	No	No effect
Citalopram	Yes	Moderate effect (dose related)
Escitalopram	Yes	Moderate effect (dose related)
Fluvoxamine	No	No effect
Fluoxetine	Yes	No effect
SNRI		
Venlafaxine	No	Low effect
Duloxetine	No	
NaRI		
Reboxetine	*No*	*No effect*
NaSSa		
Mirtazapine	No	No effect
Buspirone	No	
Methadone	Yes	QT prolonged
Buprenorphine	Yes	Less than methadone
Chlordiazepoxide	No	

Notes:

1. Drugs in italics are not on the EPUT approved formulary list.

2. SPC recommendations for ECG as of September 2019. When indicated **No *,** consult the SPC for specific clinical situations as QT prolongation can occur in high doses, polypharmacy, and in patients with established cardiovascular disease.
Shaded medications are both approved in the Trust formulary and require an ECG as stated in the SPC) (https://www.medicines.org.uk/emc/browse-medicines

3. Maudsley prescribing guidelines (12th edition) creates five categorises of risk of prolongation of QT interval.

References

1. Lambiase PD, Bono JP de, Schilling RJ, Lowe M, Turley A, Slade A, et al. British Heart Rhythm Society Clinical Practice Guidelines on the Management of Patients Developing QT Prolongation on Antipsychotic Medication. Arrhythmia Electrophysiol Rev. 2019;8(3):161–5.