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Citalopram & escitalopram:QT interval prolongation

New maximum daily dose restrictions, contraindications, and warnings

Information has been issued via Drug Safety Update, Volume 5, Issue 5, December 2011 and 'Dear Healthcare Professional Letters' for both citalopram and escitalopram regarding **new restrictions on the maximum daily doses, contraindications, and warnings.**

This is as a result of an assessment of a QT study that revealed dose-dependent increase in the QT interval observed with ECG monitoring for both citalopram and escitalopram.

Maximum licensed daily doses for citalopram and escitalopram

	Adults	Adults > 65 years	Adults with hepatic impairment
Citalopram	**40 mg**	**20 mg**	**20 mg**
Escitalopram (non-formulary)	20 mg	10 mg	10mg

The guidance in NHS Tayside is:

⇒ to review all patients on high dose* citalopram or escitalopram with aim of reducing to new maximum licensed doses (* above new maximum licensed daily doses as stated in the table above)

⇒ not to prescribe citalopram or escitalopram with other medication known to prolong the QT interval

⇒ not to prescribe citalopram and escitalopram in patients with known QT prolongation or congenital long QT syndrome

⇒ to consider alternative antidepressant in patients with cardiac disease (e.g. patients with significant bradycardia; recent myocardial infarction or decompensated heart failure)

See flow diagram on page 3 for further guidance and table below on medicines known to prolong the QT interval.

Medicines known to increase plasma levels of citalopram or escitalopram, e.g. omeprazole & some antivirals may require dose reduction of citalopram or escitalopram and should be used with caution.

It is anticipated that most dose reductions can be safely managed in primary care.

Contact patient's psychiatrist for advice if high dose treatment was initiated on the recommendation of mental health services.

Co administration of citalopram and escitalopram with medicines that prolong the QT interval is contraindicated. These include: (**NB**: This list is not exhaustive.)

Antibiotics	**Antimalarials**	**Antiarrhythmics**	Sotalol	Clomipramine	**Antipsychotics**	Pimozide
Azithromycin	Chloroquine	Amiodarone	**Antiemetics**	Dosulepin	Chlorpromazine	Risperidone
Clarithromycin	Quinine	Disopyramide	Domperidone	Doxepin	Clozapine	Quetiapine
Erythromycin	**Antivirals**	Procainamide	**Antidepressants**	Imipramine	Fluphenazine	**Others**
Levofloxacin	HIV protease inhibitors	Quinidine	Amitriptyline	Lofepramine	Haloperidol	Methadone

Note: Consider other risk factors for QTc prolongation when prescribing medicines that have the potential to prolong the QTc interval. For example; hypokalaemia, hypomagnesaemia, hypocalcaemia, stress or shock, extreme physical exertion, female gender and extremes of age (children and elderly may be more susceptible to QT changes).

Monitoring Recommendations

- Electrolyte disturbances (eg,hypokalaemia and hypomagnesaemia) should be corrected before treatment with citalopram or escitalopram. Monitoring of serum potassium & magnesium is advised, particularly in elderly patients, who may be taking diuretics or proton pump inhibitors.

- Baseline ECG should be done prior to initiation of citalopram or escitalopram in patients with cardiac disease and if prescribing above licensed maximum doses (QTc for men <440 milliseconds, females < 460 milliseconds); if QTc is prolonged **do not start citalopram or escitalopram**.

- If cardiovascular symptoms, such as palpitations, vertigo, syncope, or seizures develop during treatment, cardiac evaluation including an ECG should be undertaken to exclude a possible malignant cardiac arrhythmia.
  - If QTc interval is >500 milliseconds, treatment should be withdrawn gradually (seek advice from cardiologist / psychiatrist)
  - If QTc interval duration is between 480 milliseconds and 500 milliseconds, the balance of benefits and risks of continued treatment should be carefully considered, alongside options for dose reduction or gradual withdrawal (repeat ECG & seek advice from cardiologist / psychiatrist).

- An ECG should be undertaken every 6 months in patients on high dose citalopram or escitalopram, deemed necessary for clinical reasons (e.g. obsessive compulsive disorder (OCD) / depression not responding to other antidepressants). Document unlicensed dose and rationale in notes; evidence of informed consent from service user with capacity.
  - If the QTc is less than 480 milliseconds allow the patient to continue on the same dose (consider reducing dose to previous effective dose if possible)
  - If the QTc is between 480 and 500 milliseconds, continue but seek advice from cardiologist / psychiatrist as soon as possible.
  - If the QTc is > 500milliseconds, citalopram or escitalopram should be withdrawn gradually; seek advice from cardiologist / psychiatrist

- Patients on high dose citalopram or escitalopram, where alternative medications can be tried, but patient refusing to switch—persuade patient to reduce the dose. Undertake an ECG and seek advice from psychiatrist. Document unlicensed dose and rationale in notes; evidence of informed consent from service user with capacity.
  - If QTc is > 480 milliseconds, inform the patient and switch to a different antidepressant

Examples where switching to alternative antidepressant recommended

There is information in the Tayside Area Formulary (TAF) on how to switch to another Tayside Area Formulary antidepressant.

Contact mental health for further advice.

- Patients on combination of citalopram or escitalopram and antipsychotic medication including depot preparations: Use of citalopram with antipsychotic medication is contraindicated. Switch citalopram or escitalopram to another SSRI, for example, sertraline* and continue antipsychotic medication. In resistant cases refer to psychiatrist.

- Patients on amitriptyline for neuropathic pain and citalopram or escitalopram for depression: Amitriptyline is known to prolong the QT interval so should not be prescribed with citalopram or escitalopram. Switch citalopram or escitalopram to another SSRI, for example, sertraline* and continue amitriptyline for neuropathic pain. In resistant cases refer to psychiatrist.

- Patients with congenital long QT syndrome or known pre-existing QT interval prolongation: Switch citalopram or escitalopram to another SSRI, for example sertraline*. Seek advice from cardiologist. Consider alternative antidepressant in patients with cardiac disease (e.g. patients with significant bradycardia; recent myocardial infarction or decompensated heart failure).

* Check for any drug interactions with sertraline and manage accordingly.

Citalopram maximum dose reductions (new guidance from MHRA - November 2011)

Adapted from guidelines issued by Prof. S. Bazire , Consultant Pharmacist, Norfolk & Suffolk NHS Foundation Trust
NHS Tayside Medicines Governance Unit / Mental Health

MRHA October 2011 dose recommendations for **citalopram** due to risk of a dose-dependent QT prolongation:

- Maximum dose 40mg/d in adults and 20mg/d in the elderly and people with reduced hepatic function
- C/I with known QT prolongation, congenital long QT syndrome or taking other QT-prolonging medicines
- Caution with higher risk of developing Torsades de Pointes

If citalopram dose currently above new recommendations

Discuss with service user/patient. Consider continued need for citalopram and alternative therapies; **switch if also taking any other medicines likely to cause QTc prolongation**

Adult above 40mg/d:
Reduce dose stepwise to 40mg/d
Monitor response for 3 months

Elderly or other risk factors above 20mg/d:
Reduce dose stepwise to 20mg/d
Monitor response for 3 months

Known to need above 40mg/d (adults) or 20mg/d (elderly and reduced hepatic function)
Consider risk: benefit with service user.

No further action

Remains stable

Relapses or deteriorates

Switch if possible to different SSRI or other antidepressant
If under 18 refer to CAMHS (unlicensed use).

Relapses or deteriorates refer to specialist services

If all other options exhausted consider maintaining previously effective dose [document unlicensed dose and rationale in notes; evidence of informed consent from service user with capacity]. Reduce and monitor any risk factors. Monitor with regular ECG (e.g. initially, 6-monthly and after any medicine or dose changes) and tell service user to report any abnormal heart rate or rhythm (e.g. shortness of breath, dizziness or fainting). **If significant QT prolongation detected, must seek specialist advice and/or switch**

Escitalopram: is also associated with QT interval prolongation. Maximum dose in adults remains unchanged - 20mg daily. Adults > 65 years - maximum dose reduced to 10mg daily. Adults with hepatic impairment - 10 mg daily

Escitalopram is **non-formulary** in NHS Tayside

Medicine alternatives include:

Sertraline (optimum alternative as similar indications, low interaction propensity, good tolerability, generic, NICE approved)

Fluoxetine (beware of P450 interactions)

There is little comparative data available on QTc prolongation between other antidepressants/doses. There is no single switch method:

Depending on citalopram dose, urgency, tolerability and other medicines, reduce dose, then stop and switch and titrate according to response is safest. If in doubt, consult Mental Health Pharmacists or Ninewells Medicines Information on ext 32351 or 01382 632351

References :

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2. Table 9.2 Drugs causing QT prolongation and torsades de pointes. Baxter K. Stockley's Drug Interactions – online. Accessed via www.medicinescomplete.com on 22/12/2011.

3. Psychotropic-related QT prolongation pg 101- 105. Taylor D et al. The Maudsley Prescribing Guidelines, 10th edition, London 2009, Informa Healthcare

4. Alphabetical list of drugs that prolong the QT interval and / or induce torsades de pointes. www.azcert.org/medical-pros/drug-list/browse-drug-list.cfm. accessed on 21/12/11

5. Special alerts. Citalopram: Reports of dosage related QT interval prolongation and subsequent arrhythmia prompt reduction in maximum recommended dosage. August 2011. www.uptodate.com .Citalopram: Drug Information. Lexicomp. Copyright 1978-2011. Accessed via www.knowledge.scot.nhs.uk on 21/12/11

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