

## Drug Safety Update

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Latest advice for medicines users

# Citalopram and escitalopram: QT interval prolongation- new maximum daily dose restrictions (including in elderly patients), contraindications, and warnings

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### Summary

Citalopram and escitalopram are associated with dose-dependent QT interval prolongation and should not be used in those with: congenital long QT syndrome; known pre-existing QT interval prolongation; or in combination with other medicines that prolong the QT interval. ECG measurements should be considered for patients with cardiac disease, and electrolyte disturbances should be corrected before starting treatment. For citalopram, new restrictions on the maximum daily doses now apply: 40 mg for adults; 20 mg for patients older than 65 years; and 20 mg for those with hepatic impairment.

For escitalopram, the maximum daily dose for patients older than 65 years is now reduced to 10 mg/day; other doses remain unchanged

Citalopram, a racemic mixture of R and S citalopram, is a selective serotonin reuptake inhibitor (SSRI) indicated for the treatment of major depressive disorder, panic disorder, and obsessive compulsive disorder. Escitalopram is the S enantiomer of citalopram indicated for major depressive episodes, panic disorder with or without agoraphobia, social anxiety disorder (social phobia), generalised anxiety disorder, and obsessive compulsive disorder.

## New data for QT prolongation with citalopram and escitalopram

The potential for citalopram and escitalopram to cause QT interval prolongation has been known for some time and is reflected in the product information. However, recent data have further defined this risk and have clarified that their effects on the QT interval are dose dependent. All available data have been subject to a Europe-wide review.

For both citalopram and escitalopram, elderly patients have a higher exposure due to age-related decline in metabolism and elimination. The maximum dose of both medicines has therefore been restricted in patients older than 65 years.

### Citalopram

The data for citalopram include double-blind placebo-controlled electrocardiogram (ECG) studies. A study showed a clear dose-dependent response: the change from baseline in QTc (Fridericia-correction) was 7.5 milliseconds (90% CI 5.9. 9.1) at 20 mg/day, and 16.7 milliseconds (15.0. 18.4) at 60 mg day.

### Escitalopram

For escitalopram a dose-dependent increase in QT interval was also shown: the change from baseline in QTc (Fridericia correction) was 4.3 (90% CI: 2.2. 6.4) milliseconds with 10 mg/day and 10.7 milliseconds (90% CI: 8.6. 12.8) with 30 mg/day.

Cases of QT prolongation and ventricular arrhythmia, including Torsade de Pointes (TdP), have been reported via [the Yellow Card Scheme](#) with citalopram and escitalopram, mainly in women, those with hypokalaemia, or in those with pre-existing QT prolongation or other cardiac diseases.

## Drug interactions

### Use with drugs known to prolong QT Interval

Citalopram and escitalopram may have an additive effect to other drugs that prolong the QT interval. Coadministration of citalopram and escitalopram with medicines that prolong the QT interval is therefore contraindicated. These include:

- class IA and III antiarrhythmics (eg, amiodarone, dronedarone, quinidine)
- antipsychotics (eg, fentiazine derivatives, pimozide, haloperidol)
- tricyclic antidepressants

sparfloxacin, moxifloxacin, erythromycin IV, pentamidine, arly halofantrine) e, mizolastine) some antiretrovirals (eg, ntravir, saquinavir, lopinavir)

**Use with drugs that increase escitalopram and citalopram levels**

Patients taking concomitant medications known to increase plasma levels of escitalopram and citalopram may require a dose reduction in light of these most recent QT data. Drugs known to increase plasma concentrations of escitalopram and citalopram include some antiretroviral medications, and omeprazole and cimetidine. Details of specific interactions can be found in individual Summaries of Product Characteristics (see [the electronic Medicines Compendium](#)).

**Advice for healthcare professionals:**

Maximum daily dose schedule is as follows:

	Adults	Adults >65 years	Adults with hepatic impairment
Citalopram	40 mg*	20 mg*	20 mg*
Escitalopram	20 mg	10 mg*	10 mg

\*New (restricted) maximum daily dose.

- Patients who currently take doses higher than the new recommended daily maximum should have their treatment reviewed

**Contraindications in patients at greatest risk of QT interval prolongation:**

- Citalopram and escitalopram should not be used:
  - in patients with congenital long QT syndrome or known pre-existing QT interval prolongation
  - in combination with other medicines known to prolong the QT interval (see above)

**Cautions for use:**

- The balance of benefits and risks of citalopram and escitalopram should be considered carefully, particularly at higher doses, in patients with pre-existing risk factors for QT interval prolongation- including patients with significant bradycardia; recent acute myocardial infarction; or decompensated heart failure

**Monitoring recommendations:**

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

**Further information:**

BNF section 4.3.3 [Selective serotonin re-uptake inhibitors](#)

[October](#) and [November](#) reports of the European Pharmacovigilance Working Party

See letter sent to healthcare professionals, Oct 2011 for [citalopram](#)

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