

RGH Pharmacy E-Bulletin

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A joint initiative of the Patient Services Section and the Drug and Therapeutics Information Service of the Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia. The RGH Pharmacy E-Bulletin is distributed in electronic format on a weekly basis, and aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications.

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Changes to recommended citalopram dose & QT prolongation

Citalopram is a selective serotonin reuptake inhibitor (SSRI) indicated for major depression. Previously, the usual dose was 20 mg daily, gradually increasing after 2-4 weeks, if necessary, up to 60 mg once daily. The Australian Therapeutic Goods Administration (TGA) recently followed the U.S. Food and Drug Administration (FDA) recommendation to limit the maximum daily dosage of citalopram to 40 mg once daily. This decision followed evidence from a post-marketing study that demonstrated a significant QT prolongation effect at doses of 60 mg. The FDA suggests that studies have not show a benefit in the treatment of depression at doses higher than 40 mg once daily. The QT interval is a measure of ventricular depolarisation and repolarisation. QT measurements corrected for heart rate (QTc) over 450 msec for men and 470 msec for women are considered prolonged. Prolonging the QT interval can lead to arrhythmias and in some cases result in *Torsades de Pointes* (TdP). TdP usually terminates spontaneously but can be life threatening.

In a recent randomised, multi-centre, double-blind, placebo-controlled, crossover study, 119 subjects received citalopram 20 mg per day, citalopram 60 mg per day, or placebo. The 20 mg and 60 mg doses were found to increase the QT interval by 8.5 msec and 18.5 msec respectively. In general terms, an increase in QT interval of < 30 msec, 30-60 msec, and > 60 msec from baseline infers low, medium and high risk respectively, but however concomitant factors further increase the risk.

Risk factors for QTc elongation and TdP are considered to be:

- female gender, or increasing age
- genetic disposition (including congenital long QT syndrome, familial history of sudden death, or previous history of drug-induced QT prolongation)
- heart disease / left ventricular dysfunction
- impaired drug elimination or overdosage of drugs causing QTc prolongation
- hypokalaemia or hypomagnesaemia
- obesity

An example of the effect of concomitant risk factors was observed in a previous study of terfenadine (which was removed from the market in 1997) and ketoconazole. Terfenadine, when taken alone, was observed to prolong the QT interval by an average of 8 msec however when taken with ketoconazole the QT interval was prolonged by an average 80 msec.

In Australia, the TGA recommends the following action in regards to citalopram:

- Limit maximum dose to 40 mg once daily in patients < 65 years of age
- Limit starting dose to 10 mg once daily and maximum dose to 20 mg once daily in patients:

The FDA further recommends that hypokalaemia and hypomagnesaemia should be corrected before administering citalopram, and electrolytes should be monitored as clinically indicated. More frequent electrocardiogram (ECG) monitoring in patients with congestive heart failure, bradyarrhythmias, or patients on concomitant medications that prolong the QT interval, and patients should be advised to contact a healthcare professional immediately if they experience signs and symptoms of an abnormal heart rate or rhythm while taking citalopram

For a full list of medications that can cause QT prolongation, visit <http://www.qtdrugs.org>

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FOR FURTHER INFORMATION – CONTACT THE PHARMACY DEPARTMENT ON 82751763 or email: chris.alderman@rgh.sa.gov.au
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