Clinician Frequently Asked Questions
Citalopram Label Changes

Endorsed by Behavioral Health and Pharmacy

GroupHealth.

1. What are the new Food and Drug Administration (FDA) recommendations and label changes for citalopram?

The FDA recommendations state that citalopram may cause dose-dependent QT prolongation and doses should not exceed: [1,2]

- 20 mg per day in patients that may have increased blood levels including patients who are:
  - Greater than 60 years of age
  - With hepatic impairment
  - CYP 2C19 poor metabolizers
  - Taking concomitant CYP 2C19 inhibitors, such as cimetidine
- 40 mg per day for all other patients.

2. Should all my patients taking citalopram in doses greater than the new FDA maximum be switched to a lower dose or alternate therapy?

Group Health recommends that:

- If there is evidence of a clear clinical response, have a discussion with the patient around the risks and benefits of continued therapy including both the potential of QT prolongation with continued therapy and the worsening of anxiety or depression with discontinuation of therapy.

The FDA recommends that:

- Patients with congenital long QT syndrome, bradycardia, hypokalemia, or hyopmagnesemia, recent acute myocardial infarction, uncompensated heart failure, or taking other drugs that prolong the QT interval may be at increased risk for adverse cardiovascular outcomes.

3. What are Group Health's recommendations for EKG monitoring?

Group Health recommends that providers:

- Obtain an EKG in patients who remain on citalopram doses greater than the new FDA maximum, who have additional risk factors for QT prolongation, or are prescribed an interacting medication.
- Consider periodic follow-up EKG monitoring if:
  - Patient develops cardiovascular symptoms or electrolyte abnormalities
  - An interacting medication is prescribed
- Discontinue citalopram in patients who have consistent QTc measurements greater than 500 ms.
- Consider serum potassium and magnesium monitoring in patients at risk for electrolyte disturbances.

4. What is the evidence for QT prolongation with citalopram?

The FDA has received post-marketing reports of QT interval prolongation and Torsade de Pointes (TdP) associated with citalopram.[1,2]

The results of an unpublished, randomized, double-blind, placebo-controlled crossover study suggest that QT interval prolongation is dose-dependent (n=119).[1,2]

Citalopram Dose	Increase in QT Interval (ms)	90% Confidence Interval (ms)
20 mg/day	8.5	(6.2, 10.8)
60 mg/day	18.5	(16, 21)
40 mg/day	12.6*	(10.9, 14.3)*
*Estimate based on data for citalopram 20 mg and 60 mg doses		

5. What is the evidence for escitalpram?

The maximum recommended dose of escitalopram has not changed and is 20 mg daily (approximately equivalent to citalopram 40 mg daily). A recently updated FDA alert suggests that escitalopram may not prolong the QT interval based on data from an unpublished, randomized, double-blind, placebo-controlled crossover study (n=113).[3,4]

Escitalopram Dose	Increase in QT Interval (ms)	90% Confidence Interval (ms)
10 mg/day	4.5	(2.5, 6.4)
20 mg/day	6.6*	(5.3, 7.9)*
30 mg/day	10.7	(8.7, 12.7)
*Estimate based on data for escitalopram 10 mg and 30 mg doses		

6. What is the evidence for other SSRIs (fluoxetine, sertraline and paroxetine)?

All SSRIs have been associated with QT prolongation and TdP in case reports. It is not known whether QT prolongation is dose-dependent with other SSRIs or whether they pose any more or less risk at higher doses than citalopram.

7. What is the clinical relevance of the new citalopram drug interactions?

There are new drug interaction alerts for citalopram and CYP2C19 inhibitors based on the FDA warning. The interaction is largely theoretical and the clinical significance, especially with weak CYP2C19 inhibitors, is unknown.

A resource summarizing the available evidence for these interactions is available at: Citalopram and CYP2C19 Inhibitor Drug Interaction Summary (provider.ghc.org/open/caringForOurMembers/pharmacy/citalopram.pdf).

8. Who do I contact for more information?

- Galen Goertzen, PharmD, goertzen.g@ghc.org or 509-241-7572
- Beth Arnold, PharmD, arnold.bl@ghc.org or 206-901-4663

References:

1. FDA Drug Safety Communication: Abnormal heart rhythms associated with high doses of Celexa (citalopram hydrobromide). Available at: http://www.fda.gov/Drugs/DrugSafety/ucm269086.htm Accessed August 25, 2011.
2. Celexa® (citalopram) Product Information. Forest Pharmaceuticals. St. Louis, Miss.; August 2011.
3. FDA Drug Safety Communication: Revised recommendations for Celexa (citalopram hydrobromide) related to a potential risk of abnormal heart rhythms with high doses. Available at: http://www.fda.gov/Drugs/DrugSafety/ucm297391.htm Accessed March 28, 2012.
4. Lexapro® (escitalopram) Product Information. Forest Pharmaceuticals. St. Louis, Miss.; May 2011.