Indian Health Service
IHS National Pharmacy and Therapeutics Committee
Citalopram
February 2012

Background:
At the January 2012 NPTC meeting, the NPTC reviewed the agents for use in the treatment of depression. The selective serotonin reuptake inhibitors (SSRI) were included as part of that review. Currently, the IHS National Core Formulary (NCF) has two SSRI's on the formulary, fluoxetine and sertraline.[1] In August 2011, the FDA issued a FDA Drug Safety Communication related to the potential for abnormal heart rhythm in patients using citalopram at doses above 40mg per day.[2] The warning stated, citalopram "**should no longer be used at doses greater than 40mg per day.**" Because of this warning, the NPTC voted to develop a formulary brief to discuss this topic.

Discussion:
Citalopram is an SSRI agent used for the treatment of depression. It is available as a 10, 20 and 40mg tablet as well as a 10mg/5ml oral solution. As part of the NPTC review process for the SSRI class review, purchase history data was pulled from the pharmaceutical prime vendor (PPV) and prescription data from the IHS National Data Warehouse (NDW). Data from the PPV showed that fluoxetine and sertraline are primary market leaders within the SSRI class, followed by citalopram (Table 2) at approximately 25% of market share. The NDW data show that approximately 18% of the prescriptions for citalopram are for doses greater than 40mg.

Table 1: PPV Purchase history data for SSRI class, FY11

Generic Description	Percentage of total SSRI class
CITALOPRAM HYDROBROMIDE	24.6%
ESCITALOPRAM OXALATE	4.2%
*FLUOXETINE HCL	32.6%
FLUVOXAMINE MALEATE	0.1%
PAROXETINE HCL	10.4%
*SERTRALINE HCL	27.9%

*Sertraline and fluoxetine are on the IHS National Core Formulary (NCF).[1]

Prolongation of the QT interval on an electrocardiogram can lead to a potentially fatal abnormal heart rhythm, Torsade de Pointes (TdP). Risk factors for drug induced TdP include hypokalemia, bradycardia, CHF, baseline QT prolongation, digitalis therapy and severe hypomagnesia.[3] Reports about the potential for QT prolongation with citalopram were first published in 2008.[4] The FDA reviewed results from a randomized, multi-center, double-blind placebo-controlled, crossover study of 119 patients receiving 20mg, 60mg and placebo. A summary of the findings are represented in the Table 2. Because of this data, the FDA issued the warning against using doses above 40mg per day. The FDA also recommended a maximum dose of 20mg per day "for patients with hepatic impairment, who are greater than 60 years of age, who are CYP 2C19 poor metabolizers, or who are taking concomitant cimetidine" because of the risk of TdP.[2]

Table 2: Increase in the Corrected QT Interval for Citalopram (FDA Analysis)[2]

Citalopram Dose	Increase in QT Interval (ms)	90% Confidence Interval (ms)
20mg/day	8.5	(6.2, 10.8)
60mg/day	18.5	(16.0, 21.0)
40mg/day	12.6*	(10.9, 14.3)*

*Estimate based upon the relationship between citalopram blood concentration and QT interval.

Recommendations:
Citalopram dosing at >40mg per day makes up approximately 18% of the use of citalopram. Due to the FDA recommendation concerning the increased risk of abnormal heart rhythms associated with citalopram doses greater than 40mg, it is recommended that providers stop prescribing citalopram at doses >40mg.

If you have any questions regarding this document, please contact the NPTC at nptc1@ihs.gov.

References:

1. Indian Health Service National Core Formulary. http://www.ihs.gov/nptc/index.cfm?module=dsp_nptc_formulary; accessed February 23, 2012.
2. U.S. Food and Drug Administration. FDA Drug Safety Communication: Abnormal heart rhythms associated with high doses of Celexa (citalopram hydrobromide); http://www.fda.gov/Drugs/DrugSafety/ucm269086.htm; accessed February 23, 2012.
3. Roden DM. Drug-induced prolongation of the QT interval. *N Engl J Med.* Mar 4 2004;350(10):1013-1022.
4. Kanjanauthai S, Kanluen T, Chareonthaitawee P. Citalopram induced torsade de pointes, a rare life threatening side effect. *Int J Cardiol.* Dec 17 2008;131(1):e33-34.