Drugs that inhibit CYP2D6 that should be avoided while taking tamoxifen

Strong CYP2D6 Inhibitors	
Generic Names	**Brand Names**
Fluoxetine	Prozac®
Paroxetine	Paxil®
Quinidine	Cardioquin®
Bupropion	Wellbutrin®

Moderate CYP2D6 Inhibitors	
Generic Names	**Brand Names**
Duloxetine	Cymbalta®
Diphenhydramine	Benadryl®
Thioridazine	Mellaril®
Amiodarone	Cordarone®
Cimetidine	Tagamet®
Sertraline	Zoloft®

SSRIs and SNRIs that are not inhibitors	
Generic Names	**Brand Names**
Venlafaxine	Effexor®
Citalopram	Celexa®
Escitalopram	Lexapro®

References

1. Borges S et al. "*Quantitative effect of CYP2D6 genotype and inhibitors on tamoxifen metabolism: Implication for optimization of breast cancer treatment.*" Clin Phamacol Ther. 2006 Jul;80(1):61-74.
2. Jin Y et al. "*CYP2D6 genotype, antidepressant use, and tamoxifen metabolism during adjuvant breast cancer treatment.*" J Natl Cancer Inst. 2005 Jan 5;97(1):30-9.
3. Goetz MP et al. "*The impact of cytochrome P450 2D6 metabolism in women receiving adjuvant tamoxifen.*" Breast Cancer Res Treat. 2007 Jan;101(1):113-21.
4. Gonzalez-Santiago S et al. "*CYP2D6*4 polymorphism as blood predictive biomarker of breast cancer relapse in patients receiving adjuvant tamoxifen.*" ASCO Abstract 2007.

http://medicine.iupui.edu/clinpharm/ddis/

The information presented on this card is intended as general health information and as an educational tool. It is not intended as medical advice. Only a physician, pharmacist or other health care professional should advise a patient on the use of the medications prescribed.

Drug-Interactions With Tamoxifen

A Guide for Breast Cancer Patients and Physicians

Disease Overview – Breast Cancer

Breast cancer is the most common and lethal cancer in women. The National Cancer Institute estimates that in 2007, 178,840 new cases of breast cancer will occur, and that 40,460 women will die as a result of the disease. The lifetime risk of breast cancer for women in the United States is approximately **1 in 8**. Treatment of breast cancer now involves a number of possible drugs that are used after the radiation and chemotherapy that are utilized immediately after surgical removal of the tumor. In women who have estrogen and/or progesterone receptor positive tumors that include anti-estrogen therapies including tamoxifen, which is an antagonist of the action of estrogen in the breast, and the aromatase inhibitor class of drugs, which lower the estrogen circulating in the body by blocking the synthesis of estrogen by aromatase from androgens in fat tissue. The aromatase inhibitors do not work in women before the menopause, in whom most estrogen is made in the ovaries, but tamoxifen is effective in both pre-and post-menopausal women.

According to the most recent National Cancer Comprehensive Network breast cancer clinical practice guidelines, risk reduction therapy with tamoxifen, either alone or in conjunction with surgery or radiotherapy, is recommended for premenopausal and postmenopausal patients with estrogen receptor positive disease to prevent breast cancer recurrence. The NIH Breast Cancer Prevention Trial showed that tamoxifen given for 5 years reduces the risk of invasive breast cancer by approximately 50% after 5 years of tamoxifen therapy.

Drug Information - Tamoxifen citrate (Nolvadex®), originally manufactured by AstraZeneca (also available as a generic)

Tamoxifen is a medicine that is taken as a pill by mouth. It is called a selective estrogen receptor modulator (SERM) because it acts as a weak estrogen in some tissues like bone but as a strong antagonist of the action of estrogen in the breast. It has been FDA approved for the treatment of both early and advanced estrogen receptor positive breast cancer in pre- and post-menopausal women and in men. Tamoxifen is also FDA approved for the prevention of breast cancer in women that are at high risk for breast cancer.

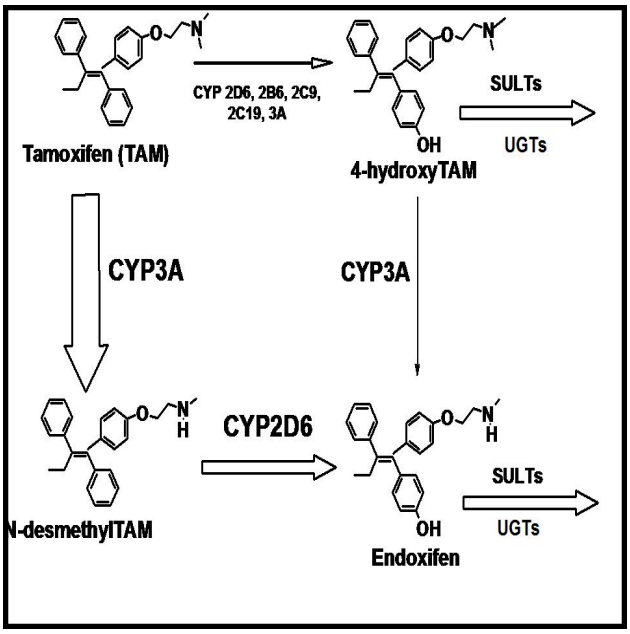
Dosing Information:

- Metastatic breast cancer: 20 to 40 mg daily
- Adjuvant treatment for breast cancer: 20 to 40 mg daily for 5 years
- Intraductal carcinoma in situ of breast, following breast surgery and radiation, to reduce risk of invasive disease: 20 mg daily for 5 years
- Breast cancer, high-risk; prophylaxis: 20 mg daily for 5 years

The product labeling contains a black box warning for serious and life-threatening events which include uterine malignancies, stroke and pulmonary embolism in patient with Ductal Carcinoma in Situ (DCIS) and women at high risk for breast cancer. Data from the largest trials conducted indicate that these events occur in 1 in every thousand women over 5 years of treatment.

Drug interactions with tamoxifen are important because the drug is extensively converted to active metabolites (breakdown products) in humans and these metabolites may be responsible for many of the effects of the drug. Since the main active metabolite is made by an enzyme in the liver called cytochrome P450 2D6 (CYP2D6), drugs that powerfully block the activity of the enzyme may reduce the effects of tamoxifen.

Tamoxifen Metabolism Pathway



We have listed here drugs that are frequently co-prescribed with tamoxifen that are powerful inhibitors of the CYP2D6 enzyme that reduce the concentrations of active metabolites substantially (Strong CYP2D6 Inhibitors), and drugs that are less powerful, but still significant inhibitors (Moderate CYP2D6 Inhibitors). Since antidepressants are so frequently co-prescribed with tamoxifen (up to 30% of patient in the US) we have specifically listed all the SSRI and SNRI antidepressants that ***do not*** interfere with tamoxifen metabolism as well as those that do.