

**March 2010**

## Drugs to Avoid While Taking Tamoxifen

Tamoxifen is an important drug for the treatment of breast cancer patients who have estrogen and/or progesterone receptor positive tumours. It is an effective drug in both pre- and post-menopausal women. Tamoxifen works by antagonizing the action of estrogen in the breast. When taken for 5 years, the risk of developing invasive breast cancer is halved following breast surgery and radiation.

Tamoxifen is a prodrug, which is converted in the liver to its active component, endoxifen, by the enzyme cytochrome P450 2D6 (CYP2D6). Drugs which block the action of CYP2D6 may reduce the activity of tamoxifen. A recent study reported online by the *British Medical Journal* found that use of paroxetine (a potent irreversible CYP2D6 inhibitor) during tamoxifen treatment is associated with an increased subsequent risk of death due to breast cancer. Tamoxifen is usually prescribed for a total duration of 5 years. The study found that there was one additional death from breast cancer for every 20 women also taking paroxetine for about 2 years while on tamoxifen therapy. Researchers at Sunnybrook Hospital in Toronto looked retrospectively at cancer mortality data. They found cancer mortality was proportional to the duration of overlap of tamoxifen with paroxetine. Compared with women with minimal treatment overlap, those overlapping 24%, 50% and 75% of the time had corresponding increases in cancer mortality of 24%, 54% and 91% (respectively).

Drugs which inhibit CYP2D6 do so by varying degrees. Some agents are strong inhibitors and generally should be avoided by women taking tamoxifen (where possible). When looking for an alternative to paroxetine in women taking tamoxifen, venlafaxine (Effexor) and mirtazepine (Remeron) have a minimal or no effect on CYP2D6 and are not expected to interact.

<b>Strong Inhibitors Avoid Use</b>	<b>Weaker Inhibitors May reduce tamoxifen efficacy</b>
fluoxetine (Prozac)	citalopram (Celexa)
paroxetine (Paxil)	sertraline (Zoloft)
duloxetine (Cymbalta)	desvenlafaxine (Pristiq)
bupropion (Wellbutrin)	
quinidine	
propafenone (Rythmol)	
amiodarone	<i>Reference: Hansten &amp; Horn's Drug Interactions Analysis &amp; Management April 2009</i>

## Neuropathy May be Linked to Excessive Use of Denture Adhesive

A report in *The Canadian Adverse Reaction Newsletter (January 2010)* described a case of a "56 year old woman who used Fixodent Original Dental Adhesive for 7 to 8 years". She was experiencing "unexplained pain, numbness and loss of sensitivity in her limbs". Similar symptoms were reported in a woman who ingested large amounts of Ultra Poli-Grip Denture Adhesive Cream "over a period of years".

Both denture adhesive products contain zinc in concentrations ranging from 17 to 34 mg/g. "Chronic, excessive ingestion of zinc can result in copper deficiency, which is an established and increasingly recognized cause of neurologic disease. This may manifest as weakness and numbness in the extremities".

*(Editor's note: On February 23, 2010, Health Canada announced that **Poli-Grip Advanced Care, Extra Strength** and **Ultra Fresh** were voluntarily withdrawn from the market due to the association of long-term, excessive use with myeloneuropathy and blood dyscrasias).*

The table which follows, lists some common drugs according to their CYP2D6 activity.



**Vyvanse® (lisdexamfetamine dimesylate)  
30 mg & 50 mg capsules  
Shire Canada** (not currently a benefit of ODB)

Vyvanse is a central nervous system stimulant indicated for the treatment of ADHD (Attention Deficit Hyperactivity Disorder) in children aged 6 to 12 years. It is a prodrug of dextroamphetamine (Dexedrine). Vyvanse is not recommended in children under 6 years of age and is not currently indicated in adolescents or adults.

**Contraindications:** Vyvanse is contraindicated:

- in advanced atherosclerosis, symptomatic cardiovascular disease, hypertension, hyperthyroidism, hypersensitivity and glaucoma
- in agitated states
- in patients with a history of drug abuse
- within 14 days following administration of monoamine oxidase inhibitors (MAOIs)

**Warnings & Precautions:**

- Growth of children may be suppressed by stimulants. Monitoring during treatment is recommended.
- Tolerance, extreme psychological dependence and severe social disability have occurred (often clinically indistinguishable from schizophrenia).
- Patients with pre-existing psychosis or comorbid bipolar disorder may experience an exacerbation of symptoms.
- Some patients may exhibit the appearance of or worsening of aggressive behaviour or hostility.
- Stimulants may lower the seizure threshold. If seizures occur during therapy, the stimulant should be discontinued.
- Amphetamines may exacerbate motor and phonic tics in Tourette's syndrome.
- Abrupt cessation of Vyvanse following administration of high doses over a prolonged period of time may result in extreme fatigue and mental depression.

**Adverse Effects:** The most common adverse effects reported include decreased appetite (39%), insomnia (18%), upper abdominal pain (12%), headache (12%), irritability (10%), weight loss (10%), vomiting (9%) and nausea (6%).

**Dose & Administration:** The recommended starting dose of Vyvanse or when switching to Vyvanse from another medication is 30 mg daily. The dose may be increased to 50 mg daily after about 1 week (if warranted). Vyvanse should be taken in the morning without regard to meals. The capsules may be swallowed whole or opened and the contents dissolved in a glass of water. If administered in a solution it should be consumed immediately (not stored).

The effectiveness of Vyvanse has not been established beyond 4 weeks in controlled trials. The efficacy of Vyvanse should be periodically evaluated during use.

**Availability & Storage:** The capsules are available in 2 strengths:

- 30 mg-white body/orange cap (imprinted S489 30 mg)
- 50 mg-white body/blue cap (imprinted S489 50 mg)

The capsules should be stored at 25°C in a tight, light-resistant container.

*(Please refer to the product monograph for complete information)*

## Discontinued ...

**Aspirin 80 mg Children's tablets** (acetylsalicylic acid delayed-release)

**Betadine Ointment** (povidone-iodine)

**Betaloc 50 & 100 mg tablets & 200 mg Durules** (metoprolol tartrate)

**Hepalean** (heparin sodium)

**Hycomine S-Pediatric Syrup 0.5 mg/ml** (hydrocodone bitartrate)

**Ogen 0.625, 1.25 & 2.5 mg tablets** (estropipate)

**Raptiva** (efalizumab)

**Vibra-Tabs 100 mg** (vibramycin)

*Emergency department visits by Ontario seniors have increased by 100,000 over 5 years to 960,000 in 2008-9. An increasing number are being discharged home or to alternate care such as long term care, instead of being admitted to hospital. (www.cihi.ca)*

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