

# Tamoxifen

Tamoxifen is a “selective estrogen receptor modulator” or SERM. In English, this means that it acts like estrogen in some tissues (bone, liver, uterus) and like an anti-estrogen in other tissues (notably, the breasts). It is used to treat metastatic breast cancer, prevent a known breast cancer from returning (adjuvant therapy), prevent breast cancer from starting in the first place (primary prevention), and sometimes used for its desirable side effects on preventing osteoporosis and lowering cholesterol.

Like all medicines, tamoxifen (trade name, Nolvadex) has side effects. Some of these side effects are serious and must be carefully considered before taking the drug. Other side effects are very rare, some are inconvenient but not dangerous, and some are ascribed to tamoxifen but may be due to something else.

The value of tamoxifen depends on the balance of good and bad effects. You should understand the benefits of any medicine before taking it. You should also know what side effects can occur, how likely they are, and whether you can (or need to) prevent these side effects.

## Benefits of Tamoxifen

In tumors that have estrogen or progesterone receptors (“ER or PR positive”), tamoxifen is used to treat metastatic disease. Sixty to 70% of women with ER or PR positive tumors respond to treatment.

Tamoxifen is used as adjuvant therapy, particularly in post-menopausal women with ER or PR positive tumors. Depending upon the receptors and menopausal status of the patient, it can reduce the chances of recurrence by up to 36%. (For ER positive premenopausal women there is a 19% improvement.)

For women who are healthy but have a “high risk” of developing cancer, tamoxifen can reduce the risk of breast cancer by 45%.

Tamoxifen can lower cholesterol and prevent heart disease. Various studies have shown:

- 1) 33-63% decrease in heart attacks
- 2) 8-15% decrease in total cholesterol
- 3) 16-26% decrease in LDL (bad guy) cholesterol

Tamoxifen helps osteoporosis:

- 1) Spine bone density increases from .4 to 2.4%
- 2) Hip bone density increases about .6%
- 3) Over all fractures are reduced by 35%

## Side effects of Tamoxifen

The following list of side effects is taken from various controlled studies. The risk of uterine cancer is doubled from approximately 1 in 1000 to 2 in 1000 women. This affects only postmenopausal women, is almost always Stage 1 when discovered, and is completely cured with hysterectomy. The best test is a pelvic exam by a gynecologist. Sometimes an ultrasound is used to measure the size of the uterine lining. If you have postmenopausal bleeding while on tamoxifen you should be checked by your doctor.

The risk of blood clots in veins increases with age. The rate for women not taking any hormones varies from 1/1000 women age 50-60 to 3-6/1000 ages 70-80. Tamoxifen

doubles the risk of blood clots to 1/100 women ages 70-80. For the most part, these clots in the leg veins are uncomfortable but not dangerous. They can be fatal if they travel to the lungs (pulmonary embolus). Women with a prior history of deep vein thrombosis or pulmonary emboli should be cautious and speak to their doctor before taking tamoxifen.

Hot flashes while on tamoxifen are more common than without the drug. In one study 56% of women on tamoxifen reported hot flashes while 43% of women taking placebo also experienced them. This suggests that there are several different causes for hot flashes in the group: stopping hormones that had prevented hot flashes, chemotherapy causing menopause, age-related menopause, etc.

In one study a vaginal discharge occurred in 22% of women on tamoxifen as opposed to 11% of women taking placebo. This discharge was generally clear and could be distinguished from an infection such as yeast. A bloody discharge should be evaluated by a physician.

In studies comparing overall quality of life, tamoxifen is not different from placebo. In fact, in one study, the control group reported feeling less feminine and having less sexual desire than the tamoxifen group. There is an average weight gain of 1.3 kg with tamoxifen compared to 1.1 kg on placebo (net 7 oz gain).

There is no increase in liver tumors with tamoxifen in humans. Studies in rats which showed such tumors do not apply to humans because rodents metabolize tamoxifen differently than people.

In the following study by Love (Love, et al. Arch Int Med 1991; 151:1842-47) 140 post menopausal women were studied. Half received placebo and the other half received Tamoxifen for 2 years. The following table shows the frequency of side effects in women taking placebo (i.e., no direct effect from drug), taking Tamoxifen, and whether the difference is significant (NS = not significant). What is most striking is the prevalence of significant symptoms in the group taking an inactive substance.

	<b>Placebo</b>	<b>Tamoxifen</b>	<b>Significance</b>
Hot Flashes	45%	67%	p<.01
Severe Hot Flashes	8%	20%	p<.04
Flushed face	33%	47%	NS
Gynecologic Symptoms*	15%	30%	p<.05
Racing heart	15%	25%	NS
Bone pain	23%	31%	NS
Joint pain	49%	52%	NS
Nausea	20%	20%	NS
Sweaty hands	21%	23%	NS
Vomiting	0%	0%	NS
Headache	50%	32%	p<.04
Insomnia	49%	55%	NS
Irritability	56%	49%	NS
Depression	36%	32%	NS
Fatigue	67%	72%	NS
Heartburn	23%	17%	NS

\*discharge, dryness, discomfort

There are anecdotal reports of other side effects including memory loss, cataracts and other visual problems. I have not been able to find controlled studies confirming or refuting these.

## **CONCLUSIONS**

As with any medicine there are advantages and disadvantages. The decision to take or not take Tamoxifen should not be based upon fear, either of the side effects or of the possibility of cancer. Many of the side effects ascribed to Tamoxifen occur frequently in a comparable group of women who are not taking the drug. This has caused undue fear of the medicine. Conversely, much of the hype in the media about breast cancer has caused unwarranted expectations that Tamoxifen is a miracle drug. The decision to take this medicine should be based upon a balance of the factual data about the drug and your clinical condition, the level of risk you are willing to take, and your ability to cope with any side effects of treatment.

The women for whom there are the largest advantages are:

- 1) those who are at risk (more than 10 %) for the return of a diagnosed cancer;
- 2) those who should not take estrogen because of prior cancer and are at risk of osteoporosis or have an elevated cholesterol;
- 3) those who have a high(er) risk of developing a new breast cancer in the future because of age, a family history of breast cancer, or a personal history of a high risk lesion.

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