

STAT CONSULT

Tamoxifen

Drug type

- Nonsteroidal agent with potent anti-estrogenic properties
- Can also be classified as a selective estrogen receptor modulator (SERM)
- Anti-estrogenic effects may be related to tamoxifen's ability to compete with estrogen for binding sites in target tissues

Pregnancy category: D

Lactation

- Unknown if excreted in breast milk
- Breast-feeding while taking tamoxifen not recommended

Black box warning

- Serious and life-threatening events associated with tamoxifen in the risk reduction setting include uterine malignancies, stroke, and pulmonary embolism
- The decision to use tamoxifen to reduce the risk of breast cancer should be based on individual assessment

Cautions and adverse effects

- Adverse reactions are relatively mild and rarely severe enough to require discontinuation of treatment
- Severe adverse reactions can sometimes be controlled by a simple reduction of dosage without loss of control of the disease
- Most frequent adverse reactions in patients with metastatic breast cancer: hot flashes, nausea, and/or vomiting
- Less frequently reported adverse reactions: vaginal bleeding, vaginal discharge, menstrual irregularities, and skin rash
- Infrequent: hypercalcemia, peripheral edema, distaste for food, pruritus vulvae, depression, dizziness, light-headedness, headache, hair thinning and/or partial hair loss, and vaginal dryness
- Tamoxifen has been associated with changes in liver enzyme levels and, rarely, fatty liver, cholestasis, hepatitis, and hepatic necrosis
- Endometriosis and uterine fibroids have been reported,



© YOAV LEVY / PHOTOTAKE

Indications

- Treatment of metastatic breast cancer in women and men
 - In premenopausal women with metastatic breast cancer, tamoxifen is alternative to oophorectomy or ovarian irradiation
 - Data suggest patients with estrogen receptor-positive tumors are more likely to benefit
- Axillary node-positive breast cancer in postmenopausal women after surgery plus irradiation
 - In some studies, most benefit to date has been in the subgroup with four or more positive axillary nodes
- Axillary node-negative breast cancer in women after surgery plus irradiation
- Reduction in risk of invasive breast cancer in women with ductal carcinoma in situ (DCIS) after surgery plus radiation
- Reduction in breast cancer incidence in high-risk women

Mechanism of action

- Competitively binds to estrogen receptors on tumors and other tissue targets, producing a nuclear complex that decreases DNA synthesis and inhibits estrogen effects
- Displays estrogeniclike effects on several sites, including the endometrium, bone, and lipids

How to administer

- Dosage is 20-40 mg/d
- To prevent or reduce the risk of breast cancer in high-risk women or women with DCIS, 20 mg once daily for 5 years
- Optimal duration of adjuvant therapy is unknown

possibly due to partial estrogenic effect of tamoxifen

- Ovarian cysts have also been observed in a small number of premenopausal patients with advanced breast cancer
- Increased bone and tumor pain and local disease flares have occurred, sometimes associated with good tumor response; patients with increased bone pain may require additional analgesics. Patients with soft tissue disease may have sudden increases in the size of pre-existing lesions, sometimes associated with marked erythema within and surrounding the lesions and/or development of new lesions. When they occur, bone pain or disease flares are seen shortly after starting tamoxifen and generally subside rapidly.
- Tamoxifen is well-tolerated in men with breast cancer and has a safety profile similar to that seen in women
 - Loss of libido and impotence have resulted in discontinuation of tamoxifen therapy in male patients
 - In oligospermic males treated with tamoxifen, LH, FSH, testosterone, and estrogen levels were elevated; no significant clinical changes were reported

Drug interactions

- Tamoxifen is metabolized into endoxifen, its primary active metabolite, via CYP2D6; strong inhibitors of CYP2D6 should be avoided, if possible
 - Moderate to strong 2D6 inhibitors include
 - Antidepressants: selective serotonin reuptake inhibitors (SSRIs) or selective noradrenergic reuptake inhibitors (SNRIs) paroxetine, fluoxetine, bupropion, duloxetine
 - Antipsychotics: thioridazine, perphenazine, pimozide
 - Cardiac drugs: quinidine, ticlopidine
- When tamoxifen is used with coumarin-type anticoagulants, significant increase in anticoagulant effect may occur; careful monitoring of prothrombin time is recommended
 - In patients receiving tamoxifen for risk reduction, tamoxifen and warfarin concurrent usage should be avoided
- Tamoxifen can also weakly inhibit hepatic cytochrome p-450 mixed function oxidases (CYP2B6, 2C8, 2C9 and 3A4)
- Herbs:
 - Avoid black cohosh and dong quai in estrogen-positive tumors
 - St John's Wort may decrease effectiveness of tamoxifen

What to tell your patient

- Tamoxifen is a hormone therapy medication classified as an anti-estrogen

- It may be given as adjuvant therapy (treatment after successful surgery) in women or men with lymph node-negative or lymph node-positive breast cancer
- Cancers with positive estrogen and progesterone receptors are more likely to respond well to tamoxifen
- It may also be prescribed for ovarian cancer
- Common side effects include hot flashes, vaginal discharge, swelling, and loss of libido (particularly in men); tell your health care provider if you experience any of these side effects
- Less common side effects include nausea, menstrual irregularities, vaginal bleeding, weight loss and mood changes; tell your health care provider if you experience any of these side effects
- A rare but serious side effect of tamoxifen is blood clots, including deep vein thrombosis and pulmonary embolus
 - Seek emergency help and notify your nurse or doctor immediately if you develop sudden chest pain and shortness of breath
 - Notify your nurse or doctor within 24 hours if you notice that one leg or arm is swollen, red, painful, and/or warm to touch and the other is not
- A rare but serious side effect of tamoxifen can be the development of uterine cancer
 - Women who have not had a hysterectomy should have regular Pap smears and pelvic examinations
 - Report abnormal vaginal bleeding to your health care provider
- Your fertility may be affected by tamoxifen
- Always tell your nurse or doctor if you experience new breast lumps or any unusual symptoms
- Before starting tamoxifen, tell your doctor about any other medications you are taking (prescription, over-the-counter, vitamins, herbal remedies, etc.)
 - Do not take aspirin, or products containing aspirin unless your doctor specifically permits this
- Let your health care professional know if you have ever had a blood clot that required medical treatment
- Inform your health care professional if you are pregnant or may be pregnant before starting this treatment; tamoxifen may be hazardous to the fetus
 - Barrier methods of contraception, such as condoms, are recommended
 - Discuss with your doctor when you may safely become pregnant or conceive a child after therapy
- Do not breast feed while taking this medication ■

Prepared by **Bette Weinstein Kaplan**. Reviewed by **Maribel Pereira, PharmD, BCPS, BCOP**.