Indications

- Treatment of metastatic breast cancer in women and men
  - In premenopausal women with metastatic breast cancer, tamoxifen is an 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 estrogenic-like 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

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,
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)
• Herbals:
  — 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

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