Anastrozole: Drug information

(For additional information see "Anastrozole: Patient drug information")

For abbreviations and symbols that may be used in Lexicomp (show table)

Brand Names: US

Arimidex

Brand Names: Canada

ACH-Anastrozole; ACT-Anastrozole; Apo-Anastrozole; Arimidex; Auro-Anastrozole; Bio-Anastrozole; JAMP-Anastrozole; Mar-Anastrozole; Med-Anastrozole; Mint-Anastrozole; Mylan-Anastrozole; Nat-Anastrozole; PMS-Anastrozole; RAN-Anastrozole; Riva-Anastrozole; Sandoz-Anastrozole; Taro-Anastrozole; Teva-Anastrozole; Zinda-Anastrozole

Pharmacologic Category

Antineoplastic Agent, Aromatase Inhibitor

Dosing: Adult

Breast cancer, advanced: Postmenopausal females: Oral: 1 mg once daily; continue until tumor progression

Breast cancer, early (adjuvant treatment): Postmenopausal females: Oral: 1 mg once daily.

Duration of therapy: The American Society of Clinical Oncology (ASCO) guidelines for Adjuvant Endocrine Therapy of Hormone-Receptor Positive Breast Cancer (Focused Update) recommend a maximum duration of 5 years of aromatase inhibitor (AI) therapy for postmenopausal women; AIs may be combined with tamoxifen for a total duration of up to 10 years of endocrine therapy. Refer to the guidelines for specific recommendations based on menopausal status and tolerability (Burstein 2014). In a phase III study with another AI (letrozole), treatment with an additional 5 years of AI therapy (for a total of 10 years of AI therapy) demonstrated a significantly improved rate of disease-free survival and a decreased risk of disease recurrence and contralateral breast cancer (when compared to placebo), although overall survival was not significantly different between groups and bone-related adverse events occurred more frequently with letrozole versus placebo (Goss 2016).

Breast cancer, risk reduction (off-label use): Postmenopausal females ≥40 years: Oral: 1 mg once daily for 5 years (Cuzick 2014)

Endometrial or uterine cancer, recurrent or metastatic (off-label use): Oral: 1 mg once daily (Rose 2000)

Ovarian cancer, recurrent (off-label use): Oral: 1 mg once daily until disease progression or unacceptable toxicity (del Carmen 2003)

Dosing: Geriatric

Refer to adult dosing.

Dosing: Renal Impairment

No dosage adjustment necessary.

Dosing: Hepatic Impairment

Mild to moderate impairment or stable hepatic cirrhosis: No dosage adjustment necessary.

Severe hepatic impairment: There are no dosage adjustments provided in the manufacturer's labeling (has not been studied).

Dosage Forms Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Tablet, Oral:

Arimidex: 1 mg

Generic: 1 mg

Generic Equivalent Available (US) Yes

Administration May be administered with or without food.

Hazardous Drugs Handling Considerations

Hazardous agent (NIOSH 2016 [group 1]).

Use appropriate precautions for receiving, handling, administration, and disposal. Gloves (single) should be worn during receiving, unpacking, and placing in storage. NIOSH recommends single gloving for administration of intact tablets or capsules (NIOSH 2016).

Use **Breast cancer:**

First-line treatment of locally-advanced or metastatic breast cancer (hormone receptor-positive or unknown) in postmenopausal women

Adjuvant treatment of early hormone receptor-positive breast cancer in postmenopausal women

Treatment of advanced breast cancer in postmenopausal women with disease progression following tamoxifen therapy

Use: Off-Label

Endometrial or uterine cancers (recurrent or metastatic); Ovarian cancer (recurrent); Risk reduction for breast cancer in postmenopausal women

Medication Safety Issues

Sound-alike/look-alike issues:

Anastrozole may be confused with anagrelide, letrozole

Arimidex may be confused with Aromasin

Adverse Reactions

>10%:

Cardiovascular: Vasodilatation (25% to 36%), ischemic heart disease (4%; 17% in patients with pre-existing ischemic heart disease), hypertension (2% to 13%), angina pectoris (2%; 12% in patients with pre-existing ischemic heart disease), edema (7% to 11%)

Central nervous system: Fatigue (19%), mood disorder (19%), headache (9% to 18%), pain (11% to 17%), depression (2% to 13%)

Dermatologic: Skin rash (6% to 11%)

Endocrine & metabolic: Hot flash (12% to 36%)

Gastrointestinal: Gastrointestinal distress (29% to 34%), nausea (11% to 20%), vomiting (8% to 13%)

Neuromuscular & skeletal: Weakness (13% to 19%), arthritis (17%), arthralgia (2% to 15%), back pain (10% to 12%), ostealgia (6% to 12%), osteoporosis (11%)

Respiratory: Pharyngitis (6% to 14%), dyspnea (8% to 11%), increased cough (7% to 11%)

1% to 10%:

Cardiovascular: Peripheral edema (5% to 10%), chest pain (5% to 7%), venous thrombosis (2% to 4%; including pulmonary embolism, thrombophlebitis, retinal vein thrombosis), myocardial infarction (1%)

Central nervous system: Insomnia (2% to 10%), dizziness (5% to 8%), paresthesia (5% to 7%), anxiety (2% to 6%), confusion (2% to 5%), drowsiness (2% to 5%), malaise (2% to 5%), nervousness (2% to 5%), carpal tunnel syndrome (3%), hypertonia (3%), cerebrovascular insufficiency (2%), lethargy (1%)

Dermatologic: Alopecia (2% to 5%), pruritus (2% to 5%), diaphoresis (1% to 5%)

Endocrine & metabolic: Hypercholesterolemia (9%), increased serum cholesterol (9%), weight gain (2% to 9%), increased gamma-glutamyl transferase (2% to 5%), weight loss (2% to 5%)

Gastrointestinal: Constipation (7% to 9%), diarrhea (7% to 9%), abdominal pain (6% to 9%), anorexia (5% to 8%), dyspepsia (7%), gastrointestinal disease (7%), xerostomia (4% to 6%)

Genitourinary: Mastalgia (2% to 8%), urinary tract infection (2% to 8%), pelvic pain (5% to 7%), vulvovaginitis (6%), vaginal dryness (1% to 5%), vaginal hemorrhage (1% to 5%), vaginal discharge (4%), vaginitis (4%), leukorrhea (2% to 3%)

Hematologic & oncologic: Lymphedema (10%), breast neoplasm (5%), neoplasm (5%), anemia (2% to 5%), leukopenia (2% to 5%), tumor flare (3%)

Hepatic: Increased serum alkaline phosphatase (2% to 5%), increased serum ALT (2% to 5%), increased serum AST (2% to 5%)

Infection: Infection (2% to 9%)

Neuromuscular & skeletal: Bone fracture (1% to 10%), arthrosis (7%), myalgia (2% to 6%), neck pain (2% to 5%), pathological fracture (2% to 5%)

Ophthalmic: Cataract (6%)

Respiratory: Flu-like symptoms (2% to 7%), sinusitis (2% to 6%), bronchitis (2% to 5%), rhinitis (2% to 5%)

Miscellaneous: Accidental injury (2% to 10%), cyst (5%), fever (2% to 5%)

<1%, postmarketing, and/or case reports: Anaphylaxis, angioedema, cerebral infarction, cerebral ischemia, decreased bone mineral density, dermal ulcer, endometrial carcinoma, erythema multiforme, hepatitis, hepatomegaly, hypercalcemia, hypersensitivity angiitis (including anaphylactoid purpura [IgA vasculitis]), increased serum bilirubin, jaundice, joint stiffness, pulmonary embolism, retinal thrombosis, skin blister, skin lesion, Stevens-Johnson syndrome, tenosynovitis (stenosing), urticaria

Contraindications Hypersensitivity to anastrozole or any component of the formulation; use in women who are or may become pregnant

Canadian labeling: Additional contraindications (not in US labeling): Lactating women

Warnings/Precautions

Concerns related to adverse effects:

• Decreased bone mineral density: Due to decreased circulating estrogen levels, anastrozole is associated with a reduction in bone mineral density (BMD); decreases (from baseline) in total hip and lumbar spine BMD have been reported. Patients with preexisting osteopenia are at higher risk for developing osteoporosis (Eastell 2008). When initiating anastrozole treatment, follow available guidelines for bone mineral density management in postmenopausal women with similar fracture risk; concurrent use of bisphosphonates may be useful in patients at risk for fractures.

• Hypercholesterolemia: Elevated total cholesterol levels (contributed to by LDL cholesterol increases) have been reported in patients receiving anastrozole; use with caution in patients with hyperlipidemias. Cholesterol levels should be monitored/managed in accordance with current guidelines for patients with LDL elevations.

Disease-related concerns:

• Hepatic impairment: Plasma concentrations in patients with stable hepatic cirrhosis were within the range of concentrations seen in normal subjects across all clinical trials. Has not been studied in patients with severe hepatic impairment.

• Ischemic disease: Patients with preexisting ischemic cardiac disease have an increased risk for ischemic cardiovascular events.

Special populations:

• Pregnancy: Use is contraindicated in women who are or may become pregnant.

• Premenopausal women: Anastrozole offers no clinical benefit in premenopausal women with breast cancer.

Metabolism/Transport Effects

Inhibits CYP1A2 (weak), CYP2C8 (weak), CYP2C9 (weak)

Drug Interactions

(For additional information: Launch drug interactions program) Lexicomp®

Amodiaquine: CYP2C8 Inhibitors may increase the serum concentration of Amodiaquine. *Risk X: Avoid combination*

CloZAPine: CYP1A2 Inhibitors (Weak) may increase the serum concentration of CloZAPine. *Risk C: Monitor therapy*

Estrogen Derivatives: May diminish the therapeutic effect of Anastrozole. *Risk X: Avoid combination*

Methadone: Aromatase Inhibitors may increase the serum concentration of Methadone. *Risk C: Monitor therapy*

Tamoxifen: May decrease the serum concentration of Anastrozole. *Risk D: Consider therapy modification*

TiZANidine: CYP1A2 Inhibitors (Weak) may increase the serum concentration of TiZANidine. Management: Avoid these combinations when possible. If combined use cannot be avoided, initiate tizanidine at an adult dose of 2 mg and increase in 2-4 mg increments based on patient response. Monitor for increased effects of tizanidine, including adverse reactions. *Risk D: Consider therapy modification*

Pregnancy Risk Factor

X (show table)

Pregnancy Implications

Adverse events were observed in animal reproduction studies. Anastrozole is contraindicated in women who are or may become pregnant (may cause fetal harm if administered during pregnancy). Use in premenopausal women with breast cancer does not provide any clinical benefit.

Breast-Feeding Considerations

It is not known if anastrozole is excreted in breast milk. Due to the potential for serious adverse reactions in the nursing infant, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of treatment to the mother.

Monitoring Parameters

Bone mineral density; total cholesterol and LDL

Breast cancer risk reduction (off-label use): Bone mineral density at baseline, mammograms, and clinical breast exam at baseline and at least every 2 years (Cuzick, 2014)

Mechanism of Action

Potent and selective nonsteroidal aromatase inhibitor. By inhibiting aromatase, the conversion of androstenedione to estrone, and testosterone to estradiol, is prevented, thereby decreasing tumor mass or delaying progression in patients with tumors responsive to hormones. Anastrozole causes an 85% decrease in estrone sulfate levels.

Pharmacodynamics/Kinetics

Onset of estradiol reduction: 70% reduction after 24 hours; 80% after 2 weeks of therapy

Duration of estradiol reduction: 6 days

Absorption: Well absorbed; extent of absorption not affected by food

Protein binding, plasma: 40%

Metabolism: Extensively hepatic (~85%) via N-dealkylation, hydroxylation, and glucuronidation; primary metabolite (triazole) inactive

Half-life elimination: ~50 hours

Time to peak, plasma: ~2 hours without food; 5 hours with food

Excretion: Feces; urine (urinary excretion accounts for ~10% of total elimination, mostly as metabolites)

Pricing: US

Tablets (Anastrozole Oral)

1 mg (30): $404.36

Tablets (Arimidex Oral)

1 mg (30): $572.84

Disclaimer: The pricing data provide a representative AWP and/or AAWP price from a single manufacturer of the brand and/or generic product, respectively. The pricing data should be used for benchmarking purposes only, and as such should not be used to set or adjudicate any prices for reimbursement or purchasing functions. Pricing data is updated monthly.

International Brand Names

A-Dex (KR); Aksastrol (UA); Alozex (BR); Altraz (IN); Anaccord (NZ); Anamidex (ID); Anarix (JO); Anarom (PH); Anaromat (RO); Anastrol (AU, IL); Anastroplex (PH); Anatero (TH, UA); Anatrole (NZ); Anazo (LK, TW, VN); Anazole (PH); Ansuzole (MY); Anzonat (SG); Aremed (MT, TH, TW); Aremed 1 (SG); Arianna (AU); Arimidex (AE, AR, AT, AU, BB, BD, BE, BF, BG, BH, BJ, BM, BO, BR, BS, BZ, CH, CI, CL, CN, CO, CR, CY, CZ, DE, DK, DO, EC, EE, ES, ET, FI, FR, GB, GH, GM, GN, GR, GT, GY, HK, HN, HR, HU, ID, IE, IL, IS, IT, JM, JO, JP, KE, KR, LB, LK, LR, LT, LU, LV, MA, ML, MR, MT, MU, MW, MX, MY, NE, NG, NI, NL, NO, NZ, PA, PE, PH, PK, PL, PR, PT, QA, RO, RU, SA, SC, SD, SE, SG, SI, SL, SN, SR, SV, TH, TN, TR, TT, TW, TZ, UG, UY, VE, VN, ZA, ZM, ZW); Ariniq (PH); Armotraz (JO); Arymideks (UA); Azonet (HR); Femistra (LK); Femizet (PH, TH); Gondonar (AR, PY); Leprofen (PY); Madelen (JO); Ozolan (RO); PMBC (LK); Sananas (PH); Trozolet (CL, EC, PY, UY, VE); Trozolite (AR); Vexal-A (PH); Zolasatin (MX); Zortex (LB)

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