Exemestane: Drug information

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

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

Brand Names: US

Aromasin

Brand Names: Canada

Aromasin; CO Exemestane

Pharmacologic Category

Antineoplastic Agent, Aromatase Inhibitor

Dosing: Adult

Breast cancer, advanced: Postmenopausal females: Oral: 25 mg once daily; continue until tumor progression

Breast cancer, early (adjuvant treatment): Postmenopausal females: Oral: 25 mg once daily (following 2 to 3 years of tamoxifen therapy) for a total duration of 5 years of endocrine therapy (in the absence of recurrence or contralateral breast cancer).

Duration of therapy: 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 aromatase inhibitor 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, early (first-line adjuvant treatment; off-label use): Postmenopausal females: Oral: 25 mg once daily for 5 years (Burstein 2010; van de Velde 2011).

Duration of therapy: 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 aromatase inhibitor 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 ≥35 years: Oral: 25 mg once daily for 5 years (Goss 2011; Visvanathan 2013)

Dosage adjustment with strong CYP3A4 inducers: 50 mg once daily when used with potent inducers (eg, rifampin, phenytoin)

Dosing: Geriatric

Refer to adult dosing.

Dosing: Renal Impairment

No adjustment necessary (although the safety of chronic doses in patients with moderate-to-severe renal impairment has not been studied, dosage adjustment does not appear necessary).

Dosing: Hepatic Impairment

No adjustment necessary (although the safety of chronic doses in patients with moderate-to-severe hepatic impairment has not been studied, dosage adjustment does not appear necessary).

Dosage Forms

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

Tablet, Oral:

Aromasin: 25 mg

Generic: 25 mg

Generic Equivalent Available (US)

Yes

Administration

Administer after a meal.

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: Treatment of advanced breast cancer in postmenopausal women whose disease has progressed following tamoxifen therapy; adjuvant treatment of postmenopausal women with estrogen receptor-positive early breast cancer following 2 to 3 years of tamoxifen (for a total of 5 consecutive years of adjuvant therapy).

Use: Off-Label

First-line adjuvant treatment of estrogen receptor-positive early breast cancer in postmenopausal women; Risk reduction for invasive breast cancer in postmenopausal women

Medication Safety Issues

Sound-alike/look-alike issues:

Aromasin may be confused with Arimidex

Exemestane may be confused with estramustine.

Adverse Reactions

Frequency not always defined. *Incidence not specifically defined, but reported in the range of 1% to 10%.

Cardiovascular: Hypertension (5% to 15%), edema (6% to 7%), ischemic heart disease (2%; angina pectoris, myocardial infarction), chest pain*

Central nervous system: Fatigue (8% to 22%), insomnia (11% to 14%), pain (13%), headache (7% to 13%), depression (6% to 13%), dizziness (8% to 10%), anxiety (4% to 10%), paresthesia (3%), carpal tunnel syndrome (2%), confusion,* hypoesthesia*

Dermatological: Hyperhidrosis (4% to 18%), alopecia (15%), dermatitis (8%), pruritus,* skin rash*

Endocrine & metabolic: Hot flash (13% to 33%), weight gain (8%), increased follicle-stimulating hormone, increased luteinizing hormone, increased sex hormone binding globulin (with daily doses of ≥2.5 mg; dose-dependent)

Gastrointestinal: Nausea (9% to 18%), abdominal pain (6% to 11%), diarrhea (4% to 10%), vomiting (7%), anorexia (6%), constipation (5%), increased appetite (3%), dyspepsia*

Genitourinary: Urinary tract infection (2% to 5%)

Hematologic & oncologic: Lymphedema*

Hepatic: Increased serum alkaline phosphatase (14% to 15%), increased serum bilirubin (5% to 7%)

Infection: Infection*

Neuromuscular & skeletal: Arthralgia (15% to 29%), back pain (9%), limb pain (9%), myalgia (6%), osteoarthritis (6%), weakness (6%), osteoporosis (5%), pathological fracture (4%), muscle cramps (2%)

Ophthalmic: Visual disturbance (5%)

Renal: Increased serum creatinine (6%)

Respiratory: Dyspnea (10%), cough (6%), flu-like symptoms (6%), bronchitis,* pharyngitis,* rhinitis,* sinusitis,* upper respiratory tract infection*

Miscellaneous: Fever (5%)

<1%, postmarketing, and/or case reports: Abnormal bone growth (osteochondrosis), acute generalized exanthematous pustulosis, cardiac failure, cholestatic hepatitis, endometrial hyperplasia, endometrial polyps, gastric ulcer, hepatitis, hypersensitivity reaction, increased gamma-glutamyl transferase, increased serum transaminases, neuropathy, tenosynovitis (fingers), thromboembolism, urticaria

Contraindications

Known hypersensitivity to exemestane or any component of the formulation

Warnings/Precautions

Concerns related to adverse effects:

• Decreased bone mineral density: Due to decreased circulating estrogen levels, exemestane is associated with a reduction in bone mineral density over time. Decreases (from baseline) in lumbar spine and femoral neck density have been observed (when compared to tamoxifen or placebo in studies where concomitant use of bisphosphonates, calcium and vitamin D were not allowed). Assess bone mineral density at baseline in patients with, or at risk for osteoporosis; monitor during exemestane therapy and initiate osteoporosis treatment if indicated.

• Lymphopenia: Grade 3 or 4 lymphopenia has been observed with exemestane, although most patients had preexisting lower grade lymphopenia; some patients improved or recovered while continuing exemestane. Lymphopenia did not result in a significant increase in viral infections, and no opportunistic infections were observed.

• Lab parameters: Elevations of AST, ALT, alkaline phosphatase, and gamma glutamyl transferase >5 times ULN have been observed (rarely) in patients with advanced breast cancer; may be attributable to underlying liver and/or bone metastases. In patients with early breast cancer, elevations of bilirubin, alkaline phosphatase, and serum creatinine were more common with exemestane treatment than with tamoxifen or placebo.

Concurrent drug therapy issues:

• Drug-drug interactions: Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detailed information. Dose adjustment recommended with concomitant strong CYP3A4 inducers.

• Estrogen-containing drugs: Exemestane should not be administered concurrently with estrogen-containing drugs.

Other warnings/precautions:

• Appropriate use: Exemestane is not indicated for use in premenopausal women.

• Vitamin D deficiency: Due to high prevalence of vitamin D deficiency in women with breast cancer, assess 25-hydroxy vitamin D levels at baseline and supplement accordingly.

Metabolism/Transport Effects

Substrate of CYP3A4 (major); **Note:** Assignment of Major/Minor substrate status based on clinically relevant drug interaction potential

Drug Interactions

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

Bosentan: May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

CYP3A4 Inducers (Moderate): May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

CYP3A4 Inducers (Strong): May decrease the serum concentration of Exemestane. Management: Exemestane U.S. product labeling recommends using an increased dose (50 mg/day) in patients receiving concurrent strong CYP3A4 inducers. The Canadian product labeling does not recommend a dose adjustment with concurrent use of strong CYP3A4 inducers. *Risk D: Consider therapy modification*

Dabrafenib: May decrease the serum concentration of CYP3A4 Substrates. Management: Seek alternatives to the CYP3A4 substrate when possible. If concomitant therapy cannot be avoided, monitor clinical effects of the substrate closely (particularly therapeutic effects). *Risk D: Consider therapy modification*

Deferasirox: May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Enzalutamide: May decrease the serum concentration of CYP3A4 Substrates. Management: Concurrent use of enzalutamide with CYP3A4 substrates that have a narrow therapeutic index should be avoided. Use of enzalutamide and any other CYP3A4 substrate should be performed with caution and close monitoring. *Risk D: Consider therapy modification*

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

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

Mitotane: May decrease the serum concentration of CYP3A4 Substrates. Management: Doses of CYP3A4 substrates may need to be adjusted substantially when used in patients being treated with mitotane. *Risk D: Consider therapy modification*

Sarilumab: May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Siltuximab: May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

St John's Wort: May decrease the serum concentration of Exemestane. Management: Exemestane US product labeling recommends using an increased dose (50 mg/day) in patients receiving St Johns Wort or strong CYP3A4 inducers. The Canadian product labeling does not recommend a dose adjustment with this combination. *Risk D: Consider therapy modification*

Tocilizumab: May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Food Interactions AUC and C_{max} were increased by 59% and 39%, respectively, when exemestane was administered with a high-fat breakfast. Management: Administer after a meal.

Pregnancy Implications Exemestane is not indicated for use in premenopausal women. Based on the mechanism of action and on animal data, exemestane is expected to cause fetal harm if administered to a pregnant woman. Women of reproductive potential should use effective contraception during treatment and for 1 month after the final dose. Pregnancy testing is recommended (for females of reproductive potential) within 7 days prior to therapy initiation.

Breast-Feeding Considerations Exemestane is indicated for use only in postmenopausal women. Due to the potential for serious adverse reactions in the breast-feeding infant, breast-feeding is not recommended by the manufacturer during treatment and for 1 month after the final dose.

Dietary Considerations Patients on aromatase inhibitor therapy should receive vitamin D and calcium supplements.

Monitoring Parameters 25-hydroxy vitamin D levels (at baseline); bone mineral density

Mechanism of Action Exemestane is an irreversible, steroidal aromatase inactivator. It is structurally related to androstenedione, and is converted to an intermediate that irreversibly blocks the active site of the aromatase enzyme, leading to inactivation ("suicide inhibition") and thus preventing conversion of androgens to estrogens in peripheral tissues. Significantly lowers circulating estrogens in postmenopausal breast cancers where growth is estrogen-dependent.

Pharmacodynamics/Kinetics

Absorption: Rapid and moderate (~42%) following oral administration; AUC and C_{max} increased by 59% and 39%, respectively, following a high-fat breakfast (compared to fasted state)

Distribution: Extensive into tissues

Protein binding: 90%, primarily to albumin and α_1-acid glycoprotein

Metabolism: Extensively hepatic; oxidation (CYP3A4) of methylene group, reduction of 17-keto group with formation of many secondary metabolites; metabolites are inactive

Half-life elimination: ~24 hours

Time to peak: Women with breast cancer: 1.2 hours

Excretion: Urine (<1% as unchanged drug, 39% to 45% as metabolites); feces (36% to 48%)

Pricing: US

Tablets (Aromasin Oral)

25 mg (30): $1103.50

Tablets (Exemestane Oral)

25 mg (30): $606.94

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 Aromacin (JO); Aromasil (ES); Aromasin (AE, AR, AT, AU, BE, BG, BH, BR, CH, CL, CN, CO, CR, CY, CZ, DE, DK, DO, EC, EE, EG, FI, GB, GR, GT, HK, HN, HR, ID, IE, IL, IQ, IR, IS, IT, KR, KW, LB, LK, LT, LU, LV, LY, MT, MY, NI, NL, NO, NZ, OM, PA, PE, PH, PL, PT, QA, RO, RU, SA, SE, SG, SI, SK, SV, SY, TH, TR, TW, UY, VE, VN, YE, ZA); Aromasine (FR); Aromastan (UA); Aromazyn (UA); Emestane (PH); Escepran (LV); Exaccord (AU); Linkotax (VN); Xtane (IN)

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