

Drug Monograph

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A - Drug Name

anastrozole

COMMON TRADE NAME(S): Arimidex®

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B - Mechanism of Action and Pharmacokinetics

Anastrozole is a potent and selective non-steroidal aromatase inhibitor which significantly lowers serum estradiol concentration. It does not have progestogenic, androgenic or estrogenic activity. In estrogen-dependent tumours, estrogen deprivation causes growth arrest and possibly tumour cell death. Anastrozole has no detectable effect on the formation of adrenal corticosteroids, aldosterone, and TSH.

Absorption	Absorption of anastrozole is rapid and maximum plasma level is reached within 2 hours of ingestion under fasting. Pharmacokinetics are linear and do not change with repeated dosing.
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Bioavailability	80%
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Effects with food	Food decreases rate but not overall extent of absorption.
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Time to reach steady state	7 days
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Distribution	Widely distributed into tissues.
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PPB	40%
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Metabolism

Extensively (85%) metabolized in liver (via N-dealkylation, hydroxylation and glucuronidation).

Active metabolites No

Inactive metabolites Yes

Elimination

Elimination mainly by metabolism (85%).

Urine 11% (unchanged), and other metabolites

Half-life 50 hours

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C - Indications and Status**Health Canada Approvals:**

- Breast cancer

Refer to the product monograph for a full list and details of approved indications.

Other Uses:

- Endometrial cancer

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D - Adverse Effects

Emetogenic Potential: Not applicable

The table below contains adverse effects reported mainly in adjuvant breast cancer with 5-year treatment. It also includes severe, life-threatening, or post-marketing adverse events from other sources.

ORGAN SITE	SIDE EFFECT* (%)	ONSET**
Cardiovascular	Arterial thromboembolism (2%)	D
	Cardiac ischemia (4%)	E
	Hypertension (13%)	D
	Lymphedema (10%)	E
	Venous thromboembolism (3%)	D
Dermatological	Erythema multiforme (rare)	E
	Rash (11%)	E
	Stevens-Johnson syndrome (rare)	E
Gastrointestinal	Abdominal pain (9%)	I E
	Nausea, vomiting (13%)	I E
	Weight changes (9%)	D
General	Fatigue (19%)	E
	Tumour flare (3%) (reported in metastatic breast cancer patients)	E
Hematological	Anemia (4%)	D
	Leukopenia (<5%)	D
Hepatobiliary	↑ LFTs (<5%) (may be severe)	D
Hypersensitivity	Hypersensitivity (rare)	I
Infection	Infection (9%)	E
Metabolic / Endocrine	Abnormal electrolyte(s) (↑Ca, rare)	E
	↑ Cholesterol (9%) (increased HDL 7%)	D
Musculoskeletal	Carpal tunnel syndrome (<10%)	E
	Fracture (10%)	D
	Musculoskeletal pain (36%)	E
	Osteoporosis (11%) (may be severe)	D
Nervous System	Dizziness (8%)	E
	Dysgeusia (rare)	E

	Headache (10%)	E
	Insomnia (10%)	E
	Mood changes (19%) (including depression)	D
	Paresthesia (7%)	E
Ophthalmic	Cataract (6%)	D
Reproductive and breast disorders	Endometrial cancer (<1%)	D
	Estrogen deprivation symptoms (36%)	E
	Vaginal bleeding (6%)	E
Respiratory	Cough, dyspnea (8%)	E
Vascular	Vasculitis (rare)	E

* "Incidence" may refer to an absolute value or the higher value from a reported range.
 "Rare" may refer to events with < 1% incidence, reported in post-marketing, phase 1 studies, isolated data or anecdotal reports.

** I = *immediate* (onset in hours to days) E = *early* (days to weeks)
 D = *delayed* (weeks to months) L = *late* (months to years)

The most common side effects for anastrozole include estrogen deprivation symptoms, musculoskeletal pain, fatigue, mood changes, hypertension, nausea, vomiting, osteoporosis, rash, fracture and headache.

Patients treated with aromatase inhibitors may be at a higher risk for **cardiovascular events** (especially in patients with pre-existing ischemic heart disease) as well as **osteoporosis**.

Joint pain/stiffness was reported with an incidence of 36% (compared to 29% in patients on tamoxifen); arthritis alone was reported with an incidence of 17%. The use of aromatase inhibitors may cause **arthralgia/arthritis**, which may impact on treatment compliance and quality of life.

In phase III studies comparing anastrozole versus megestrol acetate as second-line endocrine therapy for advanced breast cancer, the incidence of **gastrointestinal symptoms, hot flashes, vaginal dryness** and **thromboembolic disease** were similar among anastrozole and megestrol recipients. However, more patients treated with megestrol acetate reported **weight gain** as an adverse event compared to patients treated with anastrozole.

Anastrozole had statistically significant lower incidences of hot flashes, vaginal bleeding/discharge, endometrial cancer, venous thromboembolism, and ischemic cerebrovascular events than tamoxifen.

In the pivotal phase III trial comparing anastrozole and tamoxifen for adjuvant breast cancer, **fracture** rates were higher in the anastrozole group while on active treatment, but were not different after treatment completion.

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E - Dosing

Refer to protocol by which patient is being treated.

Assess patient's risk factors for osteoporosis and consider calcium and vitamin D supplements and bisphosphonates where appropriate. Refer patients to the [Bone Health During Cancer Treatment](#) pamphlet for more information.

Adults:

Oral: 1 mg Daily

Dosage with Toxicity:

Toxicity	Action
Myelosuppression	No adjustment required.
Severe hypercalcemia	Hold; discontinue if recurs.

Dosage with Hepatic Impairment:

Clearance is reduced by 30% in patients with cirrhosis, but plasma levels are within normal range.

Hepatic Impairment	Anastrozole Dose
Mild to Moderate	No adjustment is required.
Severe	Not studied; consider potential risk/benefit.

Dosage with Renal Impairment:

Clearance is reduced by 50% in severe renal impairment. However, renal excretion is a minor route of excretion and no adjustment is required.

Creatinine Clearance (mL/min)	Anastrozole Dose
≥ 30	No adjustment is required.
< 30	No adjustment is required. Consider potential risk/benefit.

Dosage in the elderly:

No dosage adjustment required.

Dosage based on ethnicity:

No dose adjustment is required. No clinically significant differences in pharmacokinetics and therapeutic responses were observed in Japanese and Caucasian patients.

Children:

Not recommended for use as safety and efficacy have not been established.

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F - Administration Guidelines

- Administer anastrozole with or without food.
- Tablets should be swallowed whole with a glass of water at the same time each day.
- Missed doses should be taken as soon as possible, but only if there are at least 12 hours before the next dose is due.
- Store at room temperature (15 to 30°C).

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G - Special Precautions

Contraindications:

- Patients with hypersensitivity to the drug or any of its components
- Pregnant or lactating women

Other Warnings/Precautions:

- Use is not recommended in pre-menopausal women*.
- Use with caution in patients with known osteoporosis or risk factors for osteoporosis, in patients with pre-existing cardiovascular disorders, severe liver or renal impairment.
- Anastrozole has not been studied in patients with brain, leptomeningeal or pulmonary lymphangitic disease.
- Use of formulations containing lactose should be carefully considered in patients with hereditary galactose intolerance, severe lactase deficiency or glucose-galactose malabsorption.

**not receiving ovarian suppression*

Other Drug Properties:

- Carcinogenicity: Unknown
Animal studies revealed increased incidences of various malignancies in both male and female populations; a non-genotoxic mechanism may play a role.

Pregnancy and Lactation:

- Teratogenicity: No
- Mutagenicity: No
- Clastogenicity: No
- Fetotoxicity: Yes

Anastrozole is **contraindicated** in pregnancy. Adequate contraception must be used by patients and their partners during treatment, and for at least **6 months** (general recommendation) after the last dose.

- Lactation: Contraindicated
- Fertility effects: Probable

Anastrozole increased pregnancy loss (increased pre- and/or post-implantation loss, increased resorption and decreased numbers of live fetuses) and produced high incidence of infertility in animal studies.

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H - Interactions

Antipyrine, cimetidine, tamoxifen and warfarin clinical interaction studies indicate that the co-administration of anastrozole with other drugs is unlikely to result in clinically significant CYP450 drug interactions. In clinical studies, there was no evidence of an interaction when anastrozole is co-administered with warfarin or bisphosphonates.

AGENT	EFFECT	MECHANISM	MANAGEMENT
Tamoxifen	↓ anastrozole concentration (by 27%)	Unknown	Do not co-administer since no efficacy or safety benefit.
Estrogen-containing or estrogenic agents	↓ estrogen suppression		Avoid.

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I - Recommended Clinical Monitoring

Treating physicians may decide to monitor more or less frequently for individual patients but should always consider recommendations from the product monograph.

Recommended Clinical Monitoring

Monitor Type	Monitor Frequency
Bone mineral density for patients at risk	Baseline and as clinically indicated
Clinical toxicity assessment for fatigue, musculoskeletal, estrogen deprivation symptoms, mood changes (including depression), rash, edema, thromboembolism, cardiovascular, GI and GU effects	At each visit

Grade toxicity using the current [NCI-CTCAE \(Common Terminology Criteria for Adverse Events\) version](#)

Suggested Clinical Monitoring

Monitor Type	Monitor Frequency
Liver function tests	Baseline and as clinically indicated
Electrolytes, including calcium	Baseline and as clinically indicated
Cholesterol and lipid evaluation	Baseline and as clinically indicated

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J - Supplementary Public Funding

ODB - General Benefit ([ODB Formulary](#))

- anastrozole

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K - References

ATAC Trialists Group. Effect of anastrozole and tamoxifen as adjuvant treatment for early-stage breast cancer: 100-month analysis of the ATAC trial. *Lancet Oncology* 2008; 9(1): 45-53.

ATAC Trialists' Group. Results of the ATAC (Arimidex, Tamoxifen, Alone or in Combination) trial after completion of 5 years' adjuvant treatment for breast cancer. *Lancet* 2005; 365: 60–2. McEvoy GK, editor.

AHFS Drug Information 2011. Bethesda: American Society of Health-System Pharmacists, p. 918-23.

Nabholtz JM, Buzdar A, Pollak M et al. Anastrozole is superior to tamoxifen as first line therapy for advanced breast cancer in postmenopausal women: results of a North American multicenter randomized trial. Arimidex Study Group. *J Clin Oncol* 2000 Nov 15;18(22):3758-67.

Product Monograph: Arimidex® (anastrozole). AstraZeneca Canada, June 30 ,2021.

April 2024 Updated Pregnancy and Lactation section

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L - Disclaimer

Refer to the [New Drug Funding Program](#) or [Ontario Public Drug Programs](#) websites for the most up-to-date public funding information.

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