

ANASTROZOL SERVYCAL

ANASTROZOLE 1 mg

Coated Tablets

Made in Argentina

Sale under filed prescription

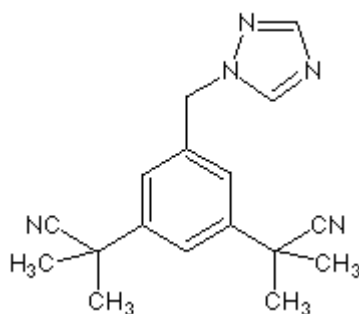
Quali-quantitative composition:

Each tablet of Anastrozol Servycal contains:

Anastrozole.....	1.00 mg
Lactose.....	47.00 mg
Microcrystalline cellulose	23.00 mg
Pregelatinized starch.....	20.00 mg
Sodium starch glycollate	3.00 mg
Povidone K-30.....	4.00 mg
Magnesium stearate	1.00 mg
Opadry II white.....	3.00 mg
Polyethylene glycol 6000	0.30 mg
Distilled water q.s. to.....	0.02 mL

Drug Description:

Anastrozole tablets for oral administration contain 1 mg of anastrozole, which is a non-steroidal aromatase inhibitor. This compound is chemically described as 1,3-Benzenediacetonitrile, $\alpha, \alpha, \alpha', \alpha'$ -tetramethyl-5-(1H-1,2,4-triazol-1-ylmethyl). Its molecular formula is $C_{17}H_{19}N_5$, and its structural formula is:



Anastrozole is a white or off-white powder that has a molecular weight of 293.4. Anastrozole is moderately soluble in water (0.5 mg/mL at 25° C), solubility is independent of pH the physiological range. Anastrozole is freely soluble in methanol, acetone, ethanol, and tetrahydrofuran, and very soluble in acetonitrile.

DRUG CATEGORY: Antineoplastic, antiestrogen (potent and selective non-steroidal aromatase inhibitor).

ATC classification: L02BG.

INDICATIONS: anastrozole is indicated for adjuvant treatment of postmenopausal women with hormone receptor positive early breast cancer.

The efficacy of this drug at early stages of cancer is based on an analysis of recurrence and disease-free survival in patients treated for a mean period of 31 months. Longer follow-up will be required to determine the efficacy of this drug in the long term.

Anastrozole is indicated as first-line therapy for postmenopausal women with hormone receptor positive or hormone receptor unknown locally advanced or metastatic breast cancer.

Anastrozole is also indicated for the treatment of advanced breast cancer in postmenopausal women with disease progression after tamoxifen treatment. Patients with estrogen receptors- negative (ER negative) breast cancer and patients who did not respond to previous tamoxifen therapy rarely responded to anastrozole.

CLINICAL PHARMACOLOGY:

Mechanism of action: many breast cancer have estrogen receptors, and growth of these tumors may be stimulated by estrogen. In postmenopausal women, the main source of circulating estrogen (mainly estradiol) is the conversion of androstenedione generated by adrenals to estrone by aromatase in peripheral tissues, such as adipose tissue, with a further conversion of estrone to estradiol.

Many breast cancers also contain aromatase but the significance of tumor-generated estrogen is uncertain.

The treatment of breast cancer has included efforts to decrease estrogen levels, by premenopausal oophorectomy and by the use of antiestrogens and progestational agents, both pre and postmenopausally. These interventions lead to decreased tumor mass or delayed progression of tumor growth in some women.

Anastrozole is a potent and selective non-steroidal aromatase inhibitor. This drug significantly lowers serum estradiol concentrations and has a no detectable effect on the formation of adrenal corticosteroids or aldosterone.

Pharmacokinetics: inhibition of aromatase activity is primarily due to anastrozole as the parent drug. Studies with radiolabeled drug have shown that anastrozole given orally is well absorbed into the systemic circulation with 83% to 85% of the radiolabeled drug recovered in urine and feces. Food does not affect the extent drug absorption. Elimination is primarily via hepatic metabolism (approximately 85%), and to a lesser extent by renal excretion (approximately 11%). Anastrozole has a mean terminal elimination half-life of 50 hours in postmenopausal women.

The main circulating metabolite of anastrozole is triazole, which lacks pharmacological activity. Pharmacokinetics parameters are similar in patients and in healthy postmenopausal volunteers.

The pharmacokinetics parameters of anastrozole are linear over a dose range of 1 to 20 mg and they do not change with repeated dosing. Consistently with mean terminal elimination half-life of 2 days, plasma concentrations reach steady-state levels at about 7 days of treatment with one daily dose of anastrozole. These steady-state levels are 3 to 4 times higher than those observed after a single dose of anastrozole.

Anastrozole is 40% bound to plasma proteins in the therapeutic range.

Metabolism and excretion: studies in postmenopausal women have demonstrated that anastrozole is extensively metabolized, with 10% of the dose excreted in the urine as

unchanged drug within 72 hs of administration, and the remainder (about 60% of the dose) is excreted in the urine as metabolites. The metabolism of anastrozole occurs by N-dealkylation, hydroxylation and glucuronidation. Three metabolites of anastrozole have been identified in plasma and human urine. The known metabolites are triazole, a glucuronide conjugate of hydroxy-anastrozole, and a glucuronide conjugate of anastrozole itself. Some minor metabolites (less than 5% of the radioactive dose) have not been identified.

Because renal elimination is not a significant route of elimination, total body clearance of anastrozole remains unchanged even in severe renal impairment (creatinine clearance less than below 30 mL/min/1.73 m²); dose adjustment is not required in patients with renal impairment or dysfunction. Dose adjustments are also unnecessary in patients with stable hepatic cirrhosis.

Special populations:

Elderly patients: anastrozole pharmacokinetics have been investigated in postmenopausal female volunteers and in patients with breast cancer. No age-related effects have been observed in patients over the range < 50 to >80 years.

Race: estradiol and estrone sulphate levels were similar between Japanese and Caucasian postmenopausal women who received 1 mg of anastrozole daily for 16 days. Minimum plasma concentrations at steady state in Japanese and Caucasian postmenopausal women were 25.7 and 30.4 ng/mL, respectively.

Renal insufficiency: anastrozole pharmacokinetics have been investigated in patients with renal insufficiency. Renal clearance decreased proportionally with creatinine clearance and was approximately 50% lower in volunteers with severe renal impairment (creatinine clearance < 30 mL/min/1.73 m²) compared to controls. Because only 10% of anastrozole is excreted in the urine as unchanged drug, the reduction in renal clearance does not influence total body clearance.

Hepatic insufficiency: hepatic metabolism accounts for 85% of anastrozole elimination. Anastrozole pharmacokinetics have been investigated in patients with hepatic cirrhosis due to alcohol abuse. The apparent oral clearance of anastrozole (CL/F) was approximately 30% lower in subjects with stable hepatic cirrhosis than in control subjects with normal hepatic function. However, plasma anastrozole concentrations in subjects with stable hepatic cirrhosis were within the range of concentrations observed in normal subjects in clinical trials. Thus, no dose adjustment is required.

Drug-Drug Interactions: anastrozole inhibits reactions catalyzed by cytochrome P450 1A2, 2C8/9, and 3A4 in vitro with Ki values, which were about 30 times higher than mean steady-state maximum concentrations values following a daily dose of 1 mg. Anastrozole has shown that it has no inhibitory effect on the reactions catalyzed by cytochrome P450 2 A6 or 2 D6 in vitro. Administration of a single dose of 30 mg/kg or multiple doses of 10 mg/kg in healthy subjects had no effect on antipyrine clearance or the urinary recovery of antipyrine metabolites. It is unlikely that the coadministration of 1 mg of anastrozole with other drugs will result in a clinically significant inhibition of metabolism mediated by cytochrome P450.

The coadministration of anastrozole and tamoxifen in patients with breast cancer reduces anastrozole plasma concentrations by 27% compared to those achieved with

anastrozole alone; however this coadministration does not affect the pharmacokinetics of tamoxifen or N-desmethyltamoxifen.

Pharmacodynamics:

Effect on estradiol: mean serum concentrations of estradiol were evaluated in clinical trials with daily doses of anastrozole of 3, 5, and 10 mg in postmenopausal women with advanced breast cancer. Suppression of serum estradiol was observed with all doses. Administration of doses of anastrozole of 1 mg or higher results in suppression of mean serum concentration of estradiol below the lower limits of detection (3.7 pmol/L). The recommended daily dose of anastrozole, 1 mg, reduced serum estradiol concentration by about 70%, and by approximately 80% after 14 days of daily dosing. The suppression of serum estradiol concentration maintained for 6 days after the interruption of daily dosing of anastrozole.

Effect on corticosteroids: in clinical trials with daily doses of anastrozole of 3, 5, and 10 mg the selectivity of the drug was determined on the basis of effects on corticosteroids synthesis. None of the doses of anastrozole affected baseline secretion of corticosteroids, aldosterone, or in response to ACTH. No glucocorticoid or mineralcorticoid replacement therapy is necessary when anastrozole is used.

Other endocrine effects: In clinical trials with multiple daily doses of 5 and 10 mg of anastrozole, and in those where thyroid stimulating hormone (TSH) was examined, no increase in TSH values was observed after anastrozole administration. Anastrozole has no direct progestogenic, androgenic or estrogenic activity in animals, but it does perturb the levels of circulating estrogens, progesterone, and androgens.

DOSAGE AND ADMINISTRATION: The usual daily dose of anastrozole is 1 mg (1 tablet per day). In patients with advanced breast cancer, anastrozole should be continued until tumor progression.

As adjuvant treatment of early breast cancer in postmenopausal women, the optimal duration of therapy is still unknown. The mean duration of therapy, on the basis of time-related data, was 31 months.

Patients with hepatic insufficiency: hepatic metabolism account for about 85% of anastrozole elimination. Although clearance of anastrozole was decreased in patients with hepatic cirrhosis due to alcohol abuse, the plasma concentrations of anastrozole remain in the same usual values or ranges for patients without liver disease. Therefore, no dose adjustment or change is recommended for patients with mild-to-moderate hepatic impairment, although these patients should be monitored for the side effects. Anastrozole has not been studied in patients with sever hepatic impairment.

Patients with renal insufficiency: no dose changes are required in patients with renal impairment.

Elderly patients: no dose adjustments are necessary in this type of patients.

CONTRAINDICATIONS: anastrozole is contraindicated in patients with hypersensitivity to the active ingredient or any of the excipients.

WARNINGS:

Anastrozole may cause fetal harm when administered in pregnant women. It has been found that anastrozole crosses the placenta after oral administration of 0.1 mg/kg. In rats and rabbits (approximately 1 and 1.9 times the recommended dose, respectively, on a

mg/m² base). Studies in both rats and rabbits at doses equal to or higher than 0.1 and 0.02 mg/kg/day, respectively (approximately 1 and 1/3, respectively, the dose recommended in humans, on a mg/m² base), administered during the organogenesis period showed that anastrozole increased pregnancy loss (increased pre and post-implantation loss, increased reabsorption, and decreased numbers of live fetuses); these effects were dose-related in rats. Placental weights were significantly increased in rats which were given doses of 0.1 mg/kg/day or higher.

Evidence of fetotoxicity, including delayed fetal development (i.e. incomplete ossification and decreased fetal body weight), was seen in rats administered doses of 1 mg/kg/day (which produced C_{ssmax} and AUC_{0-24hs} that were 19 and 9 times higher than the values found in postmenopausal volunteers at the recommended doses). No evidence of teratogenicity was found in rats administered doses of 1.0 mg/kg/day. In rabbits, anastrozole caused pregnancy failures at doses equal to or higher than 1.0 mg/kg/day (approximately 16 times the dose recommended in humans, on a mg/m² base); there was no evidence of teratogenicity in rabbits given 0.2 mg/kg/day (approximately 3 times the dose recommended in humans, on a mg/m² base).

There are no adequate and well-controlled studies on the use of anastrozole in pregnant women. If anastrozole is used in pregnant women, or if the patient becomes pregnant while receiving this drug, the patient should be advised of the potential hazard to the fetus or potential risk for loss of pregnancy.

PRECAUTIONS:

General: before commencing anastrozole treatment, pregnancy should be excluded. Anastrozole should be administered under the supervision of a qualified physician experienced in the use of antineoplastic agents.

Laboratory tests: during a clinical trial, patients receiving anastrozole showed to have more elevated serum cholesterol than those receiving tamoxifen (7% vs 3%, respectively).

Drug-drug interactions: anastrozole inhibits in vitro metabolic reactions catalyzed by cytochromes P450 1A, 2C8/9, and 3 A4 but only at relatively high concentrations. Anastrozole does not inhibit cytochrome P450 2 A6, or the polymorphic P450 2D6 in human liver microsomes. Anastrozole does not inhibit the pharmacokinetics of antipyrine. Although other no formal interaction studies have been carried out in connection with antipyrine, based on these in vivo and in vitro studies, it is unlikely that coadministration of 1 tablet of anastrozole with other drugs results in clinically significant inhibition of the metabolism of other drugs mediated by cytochrome P450.

An interaction study with warfarin showed that anastrozole has no clinically significant effect on the pharmacokinetics or the anticoagulant activity of warfarin.

According to clinical and pharmacokinetic studies with anastrozole, this drug should not be administered with tamoxifen. Coadministration of anastrozole and tamoxifen results in a reduction in anastrozole plasma levels by 27% compared with the levels achieved when anastrozole is given alone.

Therapies containing estrogens should not be used with anastrozole because they may diminish its pharmacological action.

Drugs/laboratory tests interactions: no clinically significant changes have been observed in the results of laboratory tests.

Carcinogenesis: a conventional carcinogenesis study was carried out in rats at doses of 1.0 to 25 mg/kg/day (approximately 10 to 243 times the daily maximum recommended human dose on a mg/m² base). Administration of this drug by oral gavage for 2 years revealed an increase in the incidence of hepatocellular adenoma and carcinoma and uterine stromal polyps in females and thyroid adenoma in males at high doses. An effect related to a dose increase was observed in the incidence of ovarian and uterine hyperplasia in female rats. At 25 mg/kg/day, plasma AUC_{0-24hs} levels in rats were 110 to 125 times higher than the level achieved in postmenopausal female volunteers at recommended doses.

A separate carcinogenesis study was performed in mice administered oral doses of 5 to 50 mg/kg/day (approximately 23 to 243 times the daily maximum recommended human dose on a mg/m² base) for more than two years produced an increase in the incidence of benign ovarian stromal, epithelial and granulosa cell tumors at all dose levels. A dose-related effect was the increase in the incidence of ovarian hyperplasia in females. These ovarian changes are considered to be rodent-specific effects of aromatase inhibition and are of questionable significance to humans. The incidence of lymphosarcomas was increased in males and females at high doses. At 50 mg/kg/day, plasma AUC levels in mice were 35 and 40 times higher than the level exhibited in postmenopausal volunteers at recommended doses.

Mutagenesis: anastrozole has not been found to be mutagenic in in vitro tests (Ames test and E. Coli, CHO-K1 gene mutation test), or in clastogenic test, either in vitro (test of chromosome aberrations in human lymphocytes) or in vivo (micronucleus tests in rats).

Impairment of fertility: oral administration of anastrozole in female rats (from two weeks prior to mating to day 7 of pregnancy) produced a significant incidence of infertility and reduced the number viable pregnancies at doses of 1 mg/kg/day (approximately 10 times the recommended human dose on a mg/m² base and 9 times higher than AUC_{0-24hs} found in postmenopausal volunteers at recommended doses). Pre-implementation loss of ova or fetus was increased at doses equal to or higher than 0.02 mg/kg/day (approximately 1/5 the recommended human dose on a mg/m² base). Recovery of fertility was observed after a 5-week period of non-dosing, which followed a 3-week period of dosing. It is unknown whether these effects seen in female rats are indicative of or correlate to fertility impairment in humans.

Clinical trials with multiple doses of anastrozole in rats for 6 months at doses equal to or higher than 1 mg/kg/day produced plasma C_{ssmax} and AUC_{0-24hs} which were 9-19 times higher than the respective values found in postmenopausal volunteers at recommended doses, and resulted in ovarian hypertrophy and the presence of follicular cysts. In addition, uterine hyperplasia was observed in 6-month studies in female dogs administered doses equal to or higher than 1 mg/kg/day (which produced plasma C_{ssmax} and AUC_{0-24hs} that were 22 and 16 times higher than the respective values found in postmenopausal women at recommended doses). It is unknown which of these effects on the reproductive organs of animals are associated with fertility impairment in premenopausal women.

Pregnancy: Pregnancy category D.

Breastfeeding: It is unknown whether this drug is excreted in breast milk. Because some drugs are excreted in breast milk, anastrozole should be used with caution in breastfeeding mothers.

Elderly patients: about 50% of patients recruited in two clinical trials were 65 years old or older. Patients ≥ 65 years had a moderately better tumor response and time to progression than patients < 65 years regardless of the randomized treatment.

In other two clinical trials, 50% of patients were older than 65 years old. Response rates and time to progression were similar for patients older or younger than 65 years old. In an adjuvant clinical trial, 35% of patients were under 60 years of age; 38% were ≥ 60 to ≤ 70 years old; and 27% were > 70 years old. The number of events per group was insufficient to determine efficacy.

ADVERSE REACTIONS:

Adjuvant therapy: The following adverse events occurred with an incidence of 5% during treatment, or within 14 days of the end of treatment.

BODY	%
Asthenia	17
Pain	15
Back pain	8
Headaches	9
Abdominal pain	7
Infections	7
Accidental injury	7
Flu syndrome	5
Chest pain	5
CARDIOVASCULAR	%
Vasodilatation	35
Hypertension	9
DIGESTIVE	%
Nausea	10
Constipation	7
Diarrhea	7
Dyspepsia	5
Gastrointestinal disorders	5
HEMIC-LYMPHATIC	%
Lymphoedema	9
METABOLIC-NUTRITIONAL	%
Peripheral edema	8
Weight gain	8
Hypercholesterolemia	7
MUSKULOSKELETAL	%
Arthritis	14
Arthralgia	13
Osteoporosis	7
Fractures	7
Bone pain	5
Arthrosis	6

NERVOUS SYSTEM	%
Depression	11
Insomnia	9
Dizziness	6
Anxiety	5
Paresthesia	6
RESPIRATORY	%
Pharyngitis	12
Increased cough	7
Dyspnea	6
SKIN AND APPENDAGES	%
Rash	10
Sweating	4
UROGENITAL	%
Leukorrhea	2
Urinary tract infection	6
Breast pain	7
Vulvovaginitis	6

* Episodes of non pathological fractures were more frequently observed in patients treated with anastrozole (7%).

First line treatment: The following adverse events occurred according to different clinical trials.

BODY	%
Asthenia	16
Pain	14
Back pain	12
Headaches	9
Abdominal pain	8
Chest pain	7
Flu syndrome	7
Pelvic pain	5
CARDIOVASCULAR	%
Vasodilatation	25
Hypertension	5

DIGESTIVE	%
Nausea	19
Diarrhea	9
Constipation	8
Vomits	8
Anorexia	5
METABOLIC-NUTRITIONAL	%

Peripheral edema	10
MUSCULOSKELETAL	%
Bone pain	11
NERVOUS SYSTEM	%
Dizziness	6
Insomnia	6
Depression	5
Hypertonia	3
RESPIRATORY	%
Increased cough	11
Dyspnea	10
Pharyngitis	10
SKIN AND APPENDAGES	%
Rash	8
UROGENITAL	%
Leukorrhea	9

Other adverse events were:

ADVERSE EVENT	%
Depression	5
Tumor flare	3
Thromboembolic disease	4
Venous*	
Coronary and cerebral**	
Gastrointestinal disorders	34
Hot flashes	26
Vaginal dryness	2
Lethargy	1
Vaginal bleeding	1
Weight gain	2

* Includes pulmonary embolus, thrombophlebitis, and retinal vein thrombosis.

**Includes myocardial infarction, myocardial ischemia, angina pectoris, cerebrovascular accident, and cerebral ischemia.

Second line treatment: The following adverse events occurred according to different clinical trials.

ADVERSE EVENT	%
Asthenia	16
Nausea	16
Headaches	13
Hot flashes	12
Back pain	11
Dyspnea	9
Vomits	9
Increased cough	8

Diarrhea	8
Constipation	7
Abdominal pain	7
Anorexia	7
Bone pain	6
Pharyngitis	6
Dizziness	6
Rash	6
Dry mouth	6
Peripheral edema	5
Pelvic pain	5
Depression	5
Chest pain	5
Paresthesias	5
Vaginal bleeding	2
Weight pain	2
Sweating	2
Increased appetite	0

Other less frequent adverse events (2% to 5%) were the following:

- **Body:** Flu syndrome, fever, neck pain, malaise, accidental injury, infections.
- **Hepatic:** γ GT, SGOT, and SGPT increased.
- **Hematologic:** Anemia, leukopenia.
- **Metabolic and Nutritional:** Alkaline phosphatase increased, weight gain. Serum total cholesterol levels were increased by 0.5 mmol/L among patients treated with anastrozole. Increases in LDL cholesterol may have contributed to these changes.
- **Musculoskeletal:** Myalgia, arthralgia, pathological fracture.
- **Nervous:** Somnolence, confusion, insomnia, anxiety, nervousness.
- **Respiratory:** Sinusitis, bronchitis, rhinitis.
- **Skin and appendages:** Hair thinning, pruritus.
- **Urogenital:** Urinary tract infection, breast pain.

Vaginal bleeding has been reported infrequently during the first weeks of treatment, mainly in patients who received hormone therapy prior to anastrozole. If bleeding persists, further evaluation should be considered.

During clinical trials with anastrozole and postmarketing experience joint pain and muscle stiffness have been reported in patients receiving this drug.

Anastrozole has been associated with rash and some rare cases of mucocutaneous disorders such as erythema multiforme and Stevens-Johnson syndrome.

OVERDOSAGE:

Clinical trials have been conducted with single doses higher than 60 mg administered to healthy volunteers and with doses higher than 10 mg given to postmenopausal women with advanced breast cancer; in both cases dosage was well tolerated.

It has not been established which is the single anastrozole dose that results in life-threatening symptoms for patients.

In rats, a lethal effect was observed after the administration of a single oral dose higher than 100 mg/kg (approximately 800 times the human recommended dose on a mg/m^2

base), and this dose was associated with severe irritation to the stomach (necrosis, gastritis, ulceration, and hemorrhage).

In an oral acute toxicity study in dogs, the median lethal dose was higher than 45 mg/kg/day.

There is no specific antidote to anastrozole overdose; therefore the treatment of an overdose must be symptomatic. In the management of an overdose, the multiple agents that may have been taken should be considered. Vomiting may be induced if the patient is conscious. Dialysis may be helpful because anastrozole is not highly protein bound. Control measures and general care, as well as frequent monitoring of vital signs and hospitalization are indicated in overdose cases.

If an overdose occurs, go to the nearest Hospital or contact Toxicology Centers:

Hospital de Niños Dr. Ricardo Gutiérrez: Ph: + 54 (11) 4962-6666 / 2247

Hospital Dr. Juan P. Garrahan: Ph: + 54 (11) 4941-6191 / 6012

Hospital Dr. Juan A. Fernández: Ph: + 54 (11) 4801-5555

Hospital A. Posadas: Ph: + 54 (11) 4654-6648 / 4658-777

PRESENTATION: Anastrozol Servycal is supplied in cartons containing 30 tablets.

PATIENT INFORMATION ABOUT ANASTROZOL SERVYCAL

1. WHAT IS ANASTROZOL SERVYCAL AND WHAT IS IT USED FOR?

This medicine is supplied in tablets. Each carton contains 30 tablets.

ANASTROZOL SERVYCAL is indicated for the treatment of breast cancer tumors in postmenopausal women.

2. Anastrozol Servycal must not be administered to:

Premenopausal women, who are pregnant or breastfeeding.

Patients with severe or moderate liver disorders or diseases.

Patients with severe kidney disorders or diseases.

Patients who are taking medicines containing tamoxifen or estrogen, such as hormone replacement therapy.

Children.

Patients who have presented an allergic reaction to anastrozole or any of its components.

Be particularly careful with anastrozole:

Before taking this medicine, tell your doctor if:

-You have a clinical history or an existing disease affecting your bone integrity or structure.

-You are taking any LHRH analogue (medicines used to treat certain breast diseases, gynecological disorders, and infertility).

-You are receiving tamoxifen because it may diminish anastrozole's effectiveness.

-You have any liver or kidney impairment or disease.

Anastrozole decreases the levels of female hormones, leading to bone mineral loss, what may reduce bone strength.

If you are hospitalized, tell the health care personnel that you are taking anastrozole.

Pregnancy and breastfeeding: Check with your doctor or pharmacist before using this medicine.

Use in children: Check with your doctor or pharmacist before using this medicine.

Driving and use of machinery: It is unlikely that your ability to drive vehicles or use machinery will be impaired by these tablets; however, occasionally patients may feel weak or sleepy. If this happens to you, consult your doctor.

Use of other medicines: Tell your doctor if you are using, or if you have recently used other medicine/s, even nonprescription medicines.

Certain medicines may interact with anastrozole and it may be necessary to change dosage or interrupt treatment with any of these medicines. It is especially important that you tell your doctor if you are taking any of the following medicines: tamoxifen or estrogens (female sex hormones).

3- How to take Anastrozol Servycal:

Follow these instructions unless your doctor directs otherwise.

Remember to take your medicine.

Your doctor will determine the duration of treatment with Anastrozol Servycal. Do not interrupt treatment before your doctor tells you to do so.

Usual dose:

In adults (including elderly women), the usual dose is 1 tablet daily.

In patients with mild/moderate kidney or liver impairment, the usual dose is also 1 tablet daily.

Take the complete tablet with water.

Try to take this medicine each day at the same time.

Do not stop taking your tablets even if you feel good unless your doctor tells you to do so.

a-If you take more Anastrozol Servycal than you should:

If you take a dose higher than usual, contact your doctor or nearest hospital.

In the case of an overdose or accidental ingestion, consult the Toxicology Information Service.

b-If you miss a dose of Anastrozol Servycal:

You should take Anastrozol Servycal exactly as prescribed. However, if you miss a dose, do not take an extra tablet; simply continue your usual treatment.

4. Potential adverse effects

As all other medicines, Anastrozol Servycal may produce adverse effects.

Tell your doctor if you think you have any of the following effects or if you notice any other problem with your treatment:

Very frequent ($\geq 10\%$)

Vascular disorders: Hot flashes.

Frequent ($\geq 1\%$ and $<10\%$)

General: Weakness.

Muscles and bones: Joint pain or stiffness.

Reproductive system: vaginal dryness.

Skin: hair thinning, rash.

Gastrointestinal tract: nausea, diarrhea.

Nervous system: headache.

Not frequent ($\geq 0.1\%$ and $< 1\%$)

Reproductive system: vaginal bleeding.

Metabolism: loss of appetite, increased blood cholesterol levels.

Gastrointestinal tract: vomiting.

Nervous system: somnolence.

Very infrequent ($< 0.01\%$)

Skin: Severe skin reactions (Stevens-Johnson syndrome) with injuries, ulcers or vesicles.

Allergic reaction with swelling of the face, lips, tongue and/or throat (angioedema), which may cause difficulty to swallow and/or breath. Hives.

Anastrozol Servycal decreases the levels of female hormones, leading to bone mineral loss, which may reduce bone strength and, sometimes, produce fractures.

If you notice any other reaction not included in this patient package insert, consult your doctor.

5. STORAGE:

Keep ANASTROZOL SERVYCAL out of the reach of children.

Store in a dry place, between 15° C and 30° C.

EXPIRATION:

Do not use ANASTROZOL SERVYCAL after the expiration date appearing on the carton.

STORE IN A DRY PLACE, BETWEEN 15° C AND 30° C

THIS MEDICINE SHALL BE USED UNDER MEDICAL PRESCRIPTION AND IT SHALL NOT BE REPEATED WITHOUT A NEW PRESCRIPTION

KEEP OUT OF THE REACH OF CHILDREN

Medicinal Specialty Authorized by the Argentine Ministry of Health (A.N.M.A.T.)
Certificate No. 50605

Technical Director: Pamela Carla Marcuzzi – Pharmacist- Biochemist

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