**SUMMARY OF PRODUCT CHARACTERISTICS**

**ANASOMA 1**

Anastrozole Tablets 1 mg

*$R_x$ Only*

## 1. NAME OF THE PRODUCT: Anastrozole Tablets 1 mg

**(TRADE) NAME OF PRODUCT**: **ANASOMA** 1

**STRENGTH**: 1 mg

## 2. PHARMACEUTICAL DOSAGE FORM: Film-coated tablet

## 3. QUALITATIVE AND QUANTITATIVE COMPOSITIONS:

Each film-coated tablet contains

Anastrozole Ph.Eur…….…….. 1.0 mg
Lactose monohydrate Ph. Eur…….91.0 mg

### 3.1 PHARMACEUTICAL FORM

Anastrozole Tablets 1 mg

White, biconvex film-coated, tablet debossed with 'A1' on one side and plain on the other side.

## 4. CLINICAL PARTICULARS

### 4.1 THERAPEUTIC INDICATIONS

Anastrozole is indicated for the:
• Treatment of hormone receptor-positive advanced breast cancer in postmenopausal women.
• Adjuvant treatment of hormone receptor-positive early invasive breast cancer in postmenopausal women.
• Adjuvant treatment of hormone receptor-positive early invasive breast cancer in postmenopausal women who have received 2 to 3 years of adjuvant tamoxifen.

### 4.2 POSOLOGY AND METHOD OF ADMINISTRATION

Posology
The recommended dose of Anastrozole for adults including the elderly is one 1 mg tablet once a day.
For postmenopausal women with hormone receptor-positive early invasive breast cancer, the recommended duration of adjuvant endocrine treatment is 5 years.

*Special populations*

*Paediatric population*
Anastrozole is not recommended for use in children and adolescents due to insufficient data on safety and efficacy.

*Renal impairment*

No dose change is recommended in patients with mild or moderate renal impairment. In patients with severe renal impairment, administration of Anastrozole should be performed with caution

*Hepatic impairment*

No dose change is recommended in patients with mild hepatic disease. Caution is advised in patients with moderate to severe hepatic impairment.

Method of administration

Anastrozole should be taken orally.

## 4.3 CONTRAINDICATIONS

Anastrozole is contraindicated in:
- Pregnant or breastfeeding women.
- Patients with known hypersensitivity to anastrozole or to any of the excipients used in the product

## 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

General

Anastrozole should not be used in premenopausal women. The menopause should be defined biochemically (luteinizing hormone [LH], follicle stimulating hormone [FSH], and/or estradiol levels) in any patient where there is doubt about menopausal status. There are no data to support the use of Anastrozole with LHRH analogues.

Co-administration of tamoxifen or estrogen-containing therapies with Anastrozole should be avoided as this may diminish its pharmacological action.

Effect on bone mineral density

As Anastrozole lowers circulating estrogen levels it may cause a reduction in bone mineral density with a possible consequent increased risk of fracture.

Women with osteoporosis or at risk of osteoporosis, should have their bone mineral density formally assessed at the commencement of treatment and at regular intervals thereafter. Treatment or prophylaxis for osteoporosis should be initiated as appropriate and carefully monitored. The use of specific treatments, e.g. bisphosphonates, may stop further bone mineral loss caused by Anastrozole in postmenopausal women and could be considered.

Hepatic impairment

Anastrozole has not been investigated in breast cancer patients with moderate or severe hepatic impairment. Exposure to anastrozole can be increased in subjects with hepatic impairment administration of Anastrozole in patients with moderate and severe hepatic impairment should be performed with caution. Treatment should be based on a benefit-risk evaluation for the individual patient.

Renal impairment

Anastrozole has not been investigated in breast cancer patients with severe renal impairment. Exposure to anastrozole is not increased in subjects with severe renal impairment (GRF<30ml/min); in patients with severe renal impairment, administration of Anastrozole should be performed with caution.

Paediatric population

Anastrozole is not recommended for use in children and adolescents as safety and efficacy have not been established in this group of patients.

Hypersensitivity to lactose

This product contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

## 4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

Anastrozole inhibits CYPs 1A2, 2C8/9 and 3A4 in vitro. Clinical studies with antipyrine and warfarin showed that anastrozole at a 1 mg dose did not significantly inhibit the metabolism of antipyrine and R– and S-warfarin indicating the co-administration of Anastrozole with other medicinal products is unlikely to result in clinically significant medicinal product interactions mediated by CYP enzymes.

The enzymes mediating metabolism of anastrozole have not been identified. Cimetidine, a weak, unspecific inhibitor of CYP enzymes, did not affect the plasma concentrations of anastrozole. The effect of potent CYP inhibitors is unknown.

A review of the clinical trial safety database did not reveal evidence of clinically significant interaction in patients treated with Anastrozole who also received other commonly prescribed medicinal products. There were no clinically significant interactions with bisphosphonates.

Co-administration of tamoxifen or estrogen-containing therapies with Anastrozole should be avoided as this may diminish its pharmacological action.

## 4.6 FERTILITY, PREGNANCY AND LACTATION

Pregnancy

There are no data from the use of Anastrozole in pregnant women. Studies in animals have shown reproductive toxicity. Anastrozole is contraindicated during pregnancy.

Breastfeeding

There are no data on the use of Anastrozole during lactation. Anastrozole is contraindicated during breastfeeding.

Fertility

The effects of Anastrozole on fertility in humans have not been studied. Studies in animals have shown reproductive toxicity.

## 4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Anastrozole has no or negligible influence on the ability to drive and use machines. However, asthenia and somnolence have been reported with the use of Anastrozole and

caution should be observed when driving or operating machinery while such symptoms persist.

**4.8 Undesirable effects**

Adverse reactions listed below are classified according to frequency and System Organ Class (SOC). Frequency groupings are defined according to the following convention: very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100), rare (≥ 1/10,000 to <1/1,000), and very rare (<1/10,000). The most frequently reported adverse reactions were headache, hot flushes, nausea, rash, arthralgia, joint stiffness, arthritis, and asthenia.

**Adverse reactions by System Organ Class and frequency**

| **Adverse reactions by SOC and frequency** | | |
|---|---|---|
| Metabolism and nutrition disorders | Common | Anorexia<br>Hypercholesterolaemia |
| | Uncommon | Hypercalcaemia (with or without an increase in parathyroid hormone) |
| Nervous system disorders | Very common | Headache |
| | Common | Somnolence<br>Carpal Tunnel Syndrome*<br>Sensory disturbances (including paraesthesia, taste loss and taste perversion) |
| Vascular disorders | Very common | Hot flushes |
| Gastrointestinal disorders | Very common | Nausea |
| | Common | Diarrhoea<br>Vomiting |
| Hepatobiliary disorders | Common | Increases in alkaline phosphatase, alanine aminotransferase and aspartate aminotransferase |
| | Uncommon | Increases in gamma-GT and bilirubin<br>Hepatitis |
| Skin and subcutaneous tissue disorders | Very common | Rash |
| | Common | Hair thinning (alopecia)<br>Allergic reactions |
| | Uncommon | Urticaria |

| | | |
|---|---|---|
| | Rare | Erythema multiforme<br>Anaphylactoid reaction<br>Cutaneous vasculitis (including some reports of Henoch-Schönlein purpura)** |
| | Very rare | Stevens-Johnson syndrome Angioedema |
| Musculoskeletal and connective tissue disorders | Very common | Arthralgia/joint stiffness<br>Arthritis<br>Osteoporosis |
| | Common | Bone pain<br>Myalgia |
| | Uncommon | Trigger finger |
| Reproductive system and breast disorders | Common | Vaginal dryness<br>Vaginal bleeding *** |
| General disorders and administration site conditions | Very common | Asthenia |

*Events of Carpal Tunnel Syndrome have been reported in patients receiving Anastrozole treatment in clinical trials in greater numbers than those receiving treatment with tamoxifen. However, the majority of these events occurred in patients with identifiable risk factors for the development of the condition.
**Since cutaneous vasculitis and Henoch-Schönlein purpura was not observed in ATAC, the frequency category for these events can be considered as 'Rare' (≥ 0.01% and < 0.1%) based on the worst value of the point estimate.

***Vaginal bleeding has been reported commonly, mainly in patients with advanced breast cancer during the first few weeks after changing from existing hormonal therapy to treatment with Anastrozole. If bleeding persists, further evaluation should be considered.

### 4.9 OVERDOSE

In the management of an overdose, consideration should be given to the possibility that multiple agents may have been taken. Vomiting may be induced if the patient is alert. Dialysis may be helpful because Anastrozole is not highly protein bound. General supportive care, including frequent monitoring of vital signs and close observation of the patient, is indicated.

## 5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Enzyme inhibitors, ATC code: L02B G03

### 5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action and pharmacodynamic effects

Anastrozole is a potent and highly selective non-steroidal aromatase inhibitor. In postmenopausal women, estradiol is produced primarily from the conversion of androstenedione to estrone through the aromatase enzyme complex in peripheral tissues. Estrone is subsequently converted to estradiol. Reducing circulating estradiol levels has

been shown to produce a beneficial effect in women with breast cancer. In postmenopausal women, Anastrozole at a daily dose of 1 mg produced estradiol suppression of greater than 80% using a highly sensitive assay.

Anastrozole does not possess any progestogenic, androgenic, or estrogenic activity.

Daily doses of Anastrozole up to 10 mg do not have any effect on cortisol or aldosterone secretion, measured before or after standard adrenocorticotrophic hormone (ACTH) challenge testing. Corticoid supplements are therefore not needed.

### 5.2 PHARMACOKINETIC PROPERTIES

**Absorption**

Absorption of anastrozole is rapid and maximum plasma concentrations typically occur within two hours of dosing (under fasted conditions). Food slightly decreases the rate but not the extent of absorption. The small change in the rate of absorption is not expected to result in a clinically significant effect on steady-state plasma concentrations during once daily dosing of Anastrozole tablets. Approximately 90 to 95% of plasma anastrozole steady-state concentrations are attained after 7 daily doses, and accumulation is 3- to 4-fold. There is no evidence of time or dose-dependency of anastrozole pharmacokinetic parameters.

Anastrozole pharmacokinetics are independent of age in postmenopausal women.

**Distribution**

Anastrozole is only 40% bound to plasma proteins.

**Elimination**

Anastrozole is eliminated slowly with a plasma elimination half-life of 40 to 50 hours. Anastrozole is extensively metabolised by postmenopausal women with less than 10% of the dose excreted in the urine unchanged within 72 hours of dosing. Metabolism of anastrozole occurs by N-dealkylation, hydroxylation and glucuronidation. The metabolites are excreted primarily via the urine. Triazole, the major metabolite in plasma, does not inhibit aromatase.

*Renal or hepatic impairment*

Plasma anastrozole concentrations observed during long-term efficacy trials in patients with renal impairment were within the range of plasma anastrozole concentrations seen in patients without renal impairment. In patients with severe renal impairment, administration of Anastrozole should be performed with caution.

*Paediatric population*

In boys with pubertal gynaecomastia (10-17 years), anastrozole was rapidly absorbed, was widely distributed, and was eliminated slowly with a half-life of approximately 2 days. Clearance of anastrozole was lower in girls (3-10 years) than in the older boys and exposure higher. Anastrozole in girls was widely distributed and slowly eliminated.

## 6. PHARMACEUTICAL PARTICULARS

### List of excipients

Lactose monohydrate, Sodium Starch Glycolate, Povidone K-30, Isopropyl Alcohol Magnesium Stearate, Opadry white, Purified Water.

Composition of Opadry white:
HPMC 2910/Hypromellose
Titanium Dioxide
Macrogol/PEG

**INCOMPATIBILITIES**

Not applicable.

**6.1 SHELF LIFE**

24 months

**6.2 SPECIAL PRECAUTIONS FOR STORAGE**

Do not store above 30°C. Store in original pack and protect from light.

## 7. NATURE AND CONTENTS OF CONTAINER

250 µ clear PVC film/Aluminium foil blister packs of 3x10's tablets contained in a carton

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

## 8. MARKETING AUTHORISATION HOLDER

AUROBINDO

Aurobindo Pharma Limited,
Plot No.: 2, Maitrivihar,
Ameerpet, Hyderabad-500 038,
Telangana, India.

**Address of the site responsible for release of the finished product:**

**Eugia Pharma Specialities Limited,**
Survey No. 550, 551 & 552,
Kolthur Village,
Shameerpet Mandal,
Medchal-Malkajgiri District,
Telangana, India,

9. MARKET AUTHORIZATION NUMBETR: **TAN 21 HM 0302**

10.DATE OF FIRST AUTHORIZATION: **20th August, 2021**

**11. DATE OF PREPARATION OF THIS LEAFLET**
May 2021