1.3.1.1 Professional Information for medicines for human use

SCHEDULING STATUS

S4

1 NAME OF THE MEDICINE

MYLAN ANASTROZOLE 1 mg film-coated tablets

2 QUALITIVE AND QUANTITIVE COMPOSITION

Each tablet contains 1 mg anastrozole.

Contains sugar (lactose monohydrate 93 mg).

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablets.

White, film-coated, round, biconvex tablets, debossed with “ANA” and “1” on one side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of early breast cancer in postmenopausal women.

Treatment of advanced breast cancer in postmenopausal women.

Efficacy has not been demonstrated in oestrogen receptor-negative patients unless they

have had a previous positive clinical response to tamoxifen.

4.2 Posology and method of administration

Posology

Adults including the elderly:

One 1 mg tablet to be taken orally once a day.

Children:

Not recommended for use in children.

Renal impairment:

No dose change is recommended in patients with mild or moderate renal impairment.

Hepatic impairment:

No dose change is recommended in patients with mild hepatic disease.

Method of administration

MYLAN ANASTROZOLE 1 mg should be taken orally.

4.3 Contraindications:

MYLAN ANASTROZOLE 1 mg is contra-indicated in:

- patients with hypersensitivity to the active substance or to any of the excipients of MYLAN ANASTROZOLE 1 mg (see section 6.1),
- pre-menopausal women,

- pregnant or lactating women (see section 4.6)
- patients with severe renal impairment (creatinine clearance less than 20 ml/min),
- patients with moderate or severe hepatic disease.

4.4 Special warnings and precautions for use

As MYLAN ANASTROZOLE 1 mg lowers circulating oestrogen levels it may cause a reduction in bone mineral density with a consequent increased risk of fracture. This increased risk should be managed according to treatment guidelines for managing bone health in postmenopausal women.

MYLAN ANASTROZOLE 1 mg is not recommended for use in children or in pre-menopausal women as safety and efficacy have not been established in this group of patients.

The menopause should be defined biochemically in any patient where there is doubt about hormonal status.

There are no data to support the safe use of MYLAN ANASTROZOLE 1 mg in patients with moderate or severe hepatic impairment, or patients with severe impairment of renal function (creatinine clearance less than 20 ml/min).

Lactose:

MYLAN ANASTROZOLE 1 mg contains lactose. Patients with the rare hereditary conditions of galactose intolerance e.g. galactosaemia, Lapp lactase deficiency, glucose-galactose malabsorption or fructose intolerance should not take MYLAN ANASTROZOLE 1 mg.

4.5 Interaction with other medicines and other forms of Interaction

Antipyrine and cimetidine clinical interaction studies indicate that the co-administration of MYLAN ANASTROZOLE 1 mg with other medicines is unlikely to result in clinically significant interactions mediated by cytochrome P450.

A review of the clinical trial safety database did not reveal evidence of clinically significant interaction in patients treated with MYLAN ANASTROZOLE 1 mg who also received other commonly prescribed medicines. There were no clinically significant interactions with bisphosphonates.
There is no clinical information to date on the use of MYLAN ANASTROZOLE 1 mg in combination with other anti-cancer medicines.

Tamoxifen and/or oestrogen-containing therapies should not be co-administered with MYLAN ANASTROZOLE 1 mg as they would diminish its pharmacological action.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no data from the use of MYLAN ANASTROZOLE 1 mg in pregnant women. MYLAN ANASTROZOLE 1 mg is contraindicated in pregnant women (see section 4.3).

Breastfeeding

There are no data on the use of MYLAN ANASTROZOLE 1 mg during lactation. MYLAN ANASTROZOLE 1 mg is contraindicated during breastfeeding (see section 4.3).

Fertility

The effects of MYLAN ANASTROZOLE 1 mg on fertility in humans have not been studied.

4.7 Effects on ability to drive and use machines

Asthenia and somnolence have been reported with the use of MYLAN ANASTROZOLE 1 mg and caution should be observed when driving or operating machinery while such symptoms persist.

4.8 Undesirable effects

Summary of the safety profile

The most frequently reported adverse reactions were headache, hot flushes, nausea, rash, arthralgia, joint stiffness, arthritis, and asthenia.

Tabulated list of adverse reactions

System organ class	Frequency	Adverse reactions
Blood and the lymphatic system disorders	Less Frequent	Anaemia; leucopenia with or without infection; thromboembolism and thrombophlebitis
Metabolism and nutrition disorders	Frequent	Anorexia; hypercholesterolaemia; increased appetite
	Less Frequent	Hypercalcaemia (with or without an increase in parathyroid hormone), weight gain
Psychiatric disorders	Frequent	Depression
Nervous system disorders	Frequent	Headache; dizziness; drowsiness; carpal tunnel syndrome; somnolence; sensory

System organ class	Frequency	Adverse reactions
		disturbances (including paraesthesia, taste loss and taste perversion)
	Less Frequent	Insomnia; nervousness; anxiety; confusion
Vascular disorders	Frequent	Hot flushes; flushing; peripheral oedema
	Less Frequent	Hypertension
Respiratory, thoracic and mediastinal disorders	Frequent	Chest pain; dyspnoea; cough; pharyngitis
	Less Frequent	Bronchitis; sinusitis; rhinitis
Gastrointestinal disorders	Frequent	Nausea; vomiting; diarrhoea; constipation; abdominal pain; dry mouth
Hepato-biliary disorders	Frequent	Increase in alkaline phosphatase, alanine aminotransferase and aspartate aminotransferase
	Less Frequent	Increase in gamma-GT and bilirubin; hepatitis
Skin and subcutaneous tissue disorders	Frequent	Hair thinning (alopecia); rash; sweating; allergic reactions including pruritus
	Less Frequent	Erythema multiforme; Stevens-Johnson syndrome; angioedema; urticaria and anaphylaxis; cutaneous vasculitis (including some reports of Henoch-Schönlein purpura)
Musculoskeletal, connective tissue and bone disorders	Frequent	Arthralgia; joint pain/stiffness; myalgia; back and bone pain; arthritis; osteoporosis
	Less Frequent	Trigger finger; breast pain; bone fractures

System organ class	Frequency	Adverse reactions
Reproductive system and breast disorders	Frequent	Vaginal dryness; vaginal bleeding *
General disorders and administration site conditions	Frequent	Asthenia; pain; pelvic pain
	Less Frequent	Flu syndrome

* Vaginal bleeding has been reported in patients with advanced breast cancer, previously receiving other hormonal therapy. This reflects changes in oestrogen status. If bleeding persists, further evaluation should be considered

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "6.04 Adverse Drug Reactions Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

There is no specific antidote to overdosage and treatment must be symptomatic. In the management of an overdose, consideration should be given to the possibility that multiple medicines may have been taken. Vomiting may be induced if the patient is alert. Dialysis may be helpful because MYLAN ANASTROZOLE 1 mg 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

5.1 Pharmacodynamic properties

A 21.12 Hormone inhibitors.

Anastrozole is a selective non-steroidal aromatase inhibitor. It inhibits the conversion of androstenedione to oestrone through the aromatase enzyme complex in peripheral tissues where oestrone is subsequently converted to oestradiol. In postmenopausal women, anastrozole at a daily dose of 1 mg produced oestradiol suppression of greater than 80 %. Anastrozole does not possess any progestogenic, androgenic or oestrogenic activity. Anastrozole does not have any effect on cortisol or aldosterone secretion, measured before or after standard ACTH challenge testing.

5.2 Pharmacokinetic properties

Absorption of anastrozole is rapid and maximum plasma concentrations occur after 2 hours of dosing under fasted conditions. Anastrozole is eliminated slowly with a plasma elimination half-life of 40 to 50 hours. Food decreases the rate but not the extent of absorption. Approximately 90 to 95 % of plasma anastrozole steady-state concentrations are attained after 7 daily doses. There is no evidence of time or dose-dependency of anastrozole pharmacokinetic parameters. Anastrozole pharmacokinetics are independent of age in postmenopausal women. Pharmacokinetics have not been studied in children.

Anastrozole is only 40 % bound to plasma proteins.

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, a major metabolite in plasma and urine, does not inhibit aromatase.

The apparent oral clearance of anastrozole in volunteers with mild stable hepatic cirrhosis or mild renal impairment was in the range observed in healthy volunteers.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:

lactose monohydrate

sodium starch glycolate

povidone

magnesium stearate

Film coating:

Opadry Y-1-7000 white containing:

macrogol 300

hypromellose (E5)

titanium dioxide

6.2 Incompatibilities

Not applicable

6.3 Shelf life

48 months

6.4 Special precautions for storage

Store at or below 25°C.

The blisters must be kept in the carton until required for use.

6.5 Nature and contents of container

PVC/PE/PVDC/Aluminium blister strips of 10 tablets packed into a carton box of 10, 14, 20, 28, 30, 50, 56, 60, 84, 90, 98, 100, 300 or 500 tablets per box.

6.6 Special precautions for disposal and other handling

No special requirements

7 HOLDER OF THE CERTIFICATE OF REGISTRATION

Viatris South Africa (Pty) Ltd

4, Brewery Street,

Johannesburg,

Gauteng

8 REGISTRATION NUMBER(S)

43/21.12/0590

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

7 July 2011

10 DATE OF REVISION OF TEXT

16 February 2024