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SCHEDULING STATUS:

S4

1. NAME OF THE MEDICINE

Accord Anastrozole (film coated tablets)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Accord Anastrozole tablets for oral administration contain 1 mg of anastrozole.

Contains sugar: 95,25 mg lactose monohydrate per tablet.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film coated tablets

White to off white, round, biconvex, film coated tablets with ‘AHI’ debossing on one side and plain on the other side.

4. CLINICAL PARTICLUARS

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

Adults including the elderly

The dose of Accord Anastrozole is one 1 mg tablet taken once a day.

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Special populations

Renal impairment: no dose adjustment required in patients with mild or moderate renal impairment.

Hepatic impairment: no dose adjustment with mild hepatic impairment.

Paediatric population

Not recommended for use in children.

Method of administration

For oral use.

4.3 CONTRA-INDICATIONS

- Accord Anastrozole is contra-indicated in any patient who has shown a hypersensitivity reaction to anastrozole or to any of the excipients (see section 6.1).
- Pre-menopausal women
- Patients with severe renal impairment (creatinine clearance less than 20 ml/min)
- Pregnant and lactating women
- Patients with moderate or severe hepatic disease

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

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

Women with osteoporosis or osteopenia, or at risk of osteoporosis or osteopenia, should have their bone mineral density formally assessed at the commencement of treatment and at regular intervals thereafter. Treatment or prophylaxis for osteoporosis or osteopenia should be initiated as appropriate and carefully monitored, as per local guidelines. The use of specific treatments, e.g. bisphosphonates, may stop further bone mineral loss caused by Accord Anastrozole in postmenopausal women and could be considered (see section 4.8).

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Accord Anastrozole is contra-indicated in pre-menopausal.

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 hormonal status. There are no data to support the use of anastrozole with LHRH analogues.

Co-administration of tamoxifen or estrogen-containing therapies with Accord Anastrozole should be avoided as this may diminish its pharmacological action (see section 4.5 and 5.1).

Hepatic impairment

There is no data to support the safe use of Accord Anastrozole in patients with moderate or severe hepatic impairment. Exposure to anastrozole can be increased in subjects with hepatic impairment (see section 5.2); administration of Accord Anastrozole in patients with moderate and severe hepatic impairment should be performed with caution (see section 4.2).

Renal impairment

There is no data to support the safe use of Accord Anastrozole in patients with severe impairment of renal function (creatinine clearance less than 20 ml/min) (see section 4.3).

Paediatric population

Accord Anastrozole is not recommended for use in children as safety and efficacy has not been established in these groups of patients.

Lactose monohydrate

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 INTERACTION WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTION

- Anastrozole inhibits CYPs 1A2, 2C8/9 and 3A4 *in vitro.* Antipyrine, warfarin and cimetidine clinical interaction studies indicate that co-administration of Accord Anastrozole with other medicines is unlikely to result in clinical significant interactions mediated by cytochrome P450.

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- There is no clinical information to date on the use of anastrozole in combination with other anti-cancer medicines.
- Tamoxifen and/or oestrogen containing therapies should not be co-administered with Accord Anastrozole as it would diminish its pharmacological action.

4.6 FERTILITY, PREGNANCY AND LACTATION

Accord Anastrozole is contra-indicated in pregnant and lactating women (see section 4.3).

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Asthenia, somnolence and dizziness have been reported with the use of Accord Anastrozole 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 summary of adverse reactions

System organ class	Frequency	Adverse reaction
Blood and lymphatic system disorders	Less frequent	
	Frequency unknown	Leucopenia
Immune system disorders	Less frequent	Allergic reactions including angioedema, urticaria and anaphylaxis
Metabolism and nutrition disorders	Frequent	Anorexia, Hypercholesterolaemia
	Less frequent	Hypercalcaemia (with or without an increase in parathyroid hormone)
Psychiatric disorders	Frequent	Depression
Nervous system disorders	Frequent	Headache, Carpal Tunnel Syndrome, dizziness, drowsiness, sensory disturbances

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		(including paraesthesia, taste loss and taste perversion)
	Less frequent	Somnolence
Vascular disorders	Frequent	Hot flushes, oedema
	Frequency unknown	Thrombophlebitis
Gastro-intestinal disorders	Frequent	Nausea, diarrhoea, vomiting
Hepato-biliary disorders	Frequent	Increased alkaline phosphatase, alanine aminotransferase and aspartate aminotransferase
	Less frequent	Increased gamma-GT and bilirubin, hepatitis
Skin and subcutaneous tissue disorders	Frequent	Hair thinning (alopecia), rash, allergic reactions
	Less frequent	Erythema multiforme, Stevens-Johnson syndrome, anaphylactoid reaction, cutaneous vasculitis (including some reports of Henoch-Schönlein purpura), angioedema
Musculoskeletal, connective tissue and bone disorders	Frequent	Arthralgia, joint pain/stiffness, arthritis, osteoporosis, myalgia, bone pain
	Less frequent	Trigger finger
Reproductive system and breast disorders	Frequent	Vaginal bleeding, vaginal dryness
General disorders and administration site conditions	Frequent	Asthenia, fever, flu-like syndrome

<u>Reporting of suspected adverse reactions</u>

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected

adverse reactions to SAHPRA via the Med Safety App (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on the SAHPRA website.

4.9 OVERDOSE

Refer to side effects for symptoms of overdosage.

There is no specific antidote to overdosage and treatment must be symptomatic. In the management of an overdose, consider that multiple medicines may have been taken.

Vomiting may be induced if the patient is alert. Dialysis may be helpful because Accord 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

5.1 PHARMACODYNAMIC PROPERTIES

Category and class: A 21.12 Hormone inhibitors

Pharmacotherapeutic group: Aromatase inhibitors, ATC code: L02B G03

Mechanism of Action

Anastrozole is a selective non-steroidal aromatase inhibitor.

Anastrozole is a selective non-steroidal aromatase inhibitor. It inhibits the conversion of androstenedione to estrone through the aromatase enzyme complex in peripheral tissues where estrone 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 estrogenic activity.

It significantly lowers serum estradiol concentrations and has no detectable effect on formation of adrenal corticosteroids or aldosterone, measured before or after standard ACTH challenge testing.

5.2 PHARMACOKINETIC PROPERTIES

Anastrozole is rapidly and almost completely adsorbed from the gastro-intestinal tract following oral administration, with peak plasma concentrations occurring within about 2 hours, under fasting conditions.

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Food decreases the rate of absorption, though this is not considered clinically significant. It is metabolised in the liver, and excreted in urine, chiefly as metabolites. The terminal elimination half-life is about 50 hours, and approximately 90-95 % of plasma anastrozole steady-state concentrations are achieved after about 7 days in patients receiving once-daily doses. Anastrozole is about 40 % bound to plasma protein.

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 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

Lactose monohydrate

Povidone K-30

Sodium starch glycolate

Magnesium stearate

Film coating:

Hydroxypropyl methyl cellulose

Macrogol 300

Titanium dioxide

6.2 INCOMPATIBILITIES

Not applicable.

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6.3 SHELF-LIFE

3 years

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store at or below 25 °C.

Do not remove from outer container until required for use.

6.5 NATURE AND CONTENTS OF CONTAINER

Accord Anastrozole tablets are packaged in a plain aluminium blister foil with a clear PVC film coated PVDC.

There are 3 blister strips of 10 tablets each, packed in an outer cardboard box as a pack size of 30 tablets.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Accord Healthcare (Pty) Ltd

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8. REGISTRATION NUMBERS

42/21.12/0259

9. DATE OF FIRST AUTHORISATION

26 November 2010

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10. DATE OF REVISION OF THE TEXT

05 February 2015
11 December 2025