Applicant: Teva Pharmaceuticals (Pty) Ltd
Product name: BICALUTAMIDE 50/150 TEVA
Dosage form & strength: Each film-coated tablet contains 50 mg and 150 mg of bicalutamide, respectively
Registration Numbers: 43/21.12/0764 ; 43/21.12/0765

PROFESSIONAL INFORMATION:

SCHEDULING STATUS:

S4

1. NAME OF THE MEDICINE:

BICALUTAMIDE 50 TEVA (Film-coated tablets)

BICALUTAMIDE 150 TEVA (Film-coated tablets)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Each film-coated tablet contains 50 mg bicalutamide as active ingredient.

Contains sugar: lactose monohydrate 35 mg per tablet.

Each film-coated tablet contains 150 mg bicalutamide as active ingredient.

Contains sugar: lactose monohydrate 105 mg per tablet.

For full list of excipients, **see section 6.1**.

3. PHARMACEUTICAL FORM:

BICALUTAMIDE 50 TEVA: White to off-white, film-coated round, biconvex tablet, debossed with '93' on one side and '220' on the other.

BICALUTAMIDE 150 TEVA: White to off-white, film-coated round, biconvex tablet, one side debossed with 'BCL', plain on the other.

4. CLINICAL PARTICULARS:

4.1 Therapeutic indications:

BICULATAMIDE 50 TEVA:

The treatment of advanced prostate cancer in combination with Luteinising Hormone Release Hormone (LHRH) analogue therapy or surgical castration.

BICALUTAMIDE 150 TEVA:

In patients with locally advanced prostate cancer (T3-4, any N, M0/T1-2, N+, M0) BICALUTAMIDE 150 TEVA Is indicated as immediate therapy either alone or as adjuvant to treatment by radical prostatectomy or radiotherapy.

BICALUTAMIDE 150 TEVA is indicated as monotherapy for the management of patients with locally advanced, non-metastatic prostate cancer for whom surgical or medical castration is not appropriate.

4.2 Posology and method of administration:

Posology:

BICALUTAMIDE 50 TEVA:

Adult males (including the elderly):

One tablet (50 mg) once daily. Treatment with BICALUTAMIDE 50 TEVA should be started at least three days prior to commencing treatment with a LHRH analogue, or at the same time as surgical castration.

BICALUTAMIDE 50 TEVA:

Adult males (including the elderly):

One tablet (150 mg) once daily for two years or until progression.

Renal impairment:

No dosage adjustments required.

Hepatic impairment:

No dosage reduction required for patients with mild hepatic impairment. Increased accumulation may occur in patients with moderate to severe impairment.

4.3 Contraindications:

BICALUTAMIDE TEVA is contraindicated in:

- Patients with a known hypersensitivity towards bicalutamide or any of the excipients of BICALUTAMIDE TEVA
- Females
- Children
- Pregnant women
- Nursing mothers.

4.4 Special warnings and precautions for use:

Since BICALUTAMIDE TEVA is extensively metabolised in the liver, metabolism may be delayed in patients with moderate to severe hepatic function impairment, resulting in prolonged elimination half-life and increased risk of toxicity. Periodic assessment of hepatic function should be considered during long term use of BICALUTAMIDE TEVA. Caution should be exercised with the co-administration of BICALUTAMIDE TEVA with medicines metabolised by cytochrome P450 (see **section 4.5**). BICALUTAMIDE TEVA can increase the risk of non-alcoholic fatty liver disease (NAFLD) and associated liver disease.

BICALUTAMIDE TEVA contains lactose monohydrate. Patients with rare hereditary conditions of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take BICALUTAMIDE TEVA.

Caution should be exercised in patients with lactose intolerance.

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially ‘sodium-free’.

4.5 Interaction with other medicines and other forms of interaction:

Caution and increased monitoring of prothrombin time [PT] or International Normalised Ratio [INR] are recommended if treatment with BICALUTAMIDE TEVA is initiated in a patient stabilised on a coumarin-derivative anticoagulant. BICALUTAMIDE TEVA may displace coumarin anticoagulants, such as warfarin, from their protein binding sites. Adjustment of anticoagulant dosage may be necessary.

Concurrent administration of BICALUTAMIDE TEVA with agents that may inhibit oxidation of the bicalutamide e.g. ketoconazole and cimetidine, can lead to increased concentrations of bicalutamide and caution should be exercised.

Medication with a narrow therapeutic index (e.g. cisapride, cyclosporine and astemizole) predominantly metabolised by CYP 3A4 should be used with caution when administered with BICALUTAMIDE TEVA.

Medicines metabolised by cytochrome P450.

Although clinical studies using antipyrine as a marker of cytochrome P450 (CYP) activity showed no evidence of an interaction potential with BICALUTAMIDE TEVA, midazolam exposure (AUC) was increased by up to 80 %, after co-administration with BICALUTAMIDE TEVA for 28 days. This rise is comparable to that seen in other studies after administration of grapefruit juice.

Caution should be exercised with the co-administration of BICALUTAMIDE TEVA with compounds such as these, (see **section 4.4**).

4.6 Fertility, pregnancy and lactation:

BICALUTAMIDE TEVA is contraindicated in pregnant women and breastfeeding mothers (see **section 4.3**).

4.7 Effects on ability to drive and use machines:

BICALUTAMIDE TEVA has no effect on the ability to drive or operate machinery.

4.8 Undesirable effects:

b. TABULATED LIST OF ADVERSE REACTIONS:

SYSTEM ORGAN CLASS:	**FREQUENCY:**	**EVENT:**
Infections and infestations	Frequent	Infection, including pulmonary and upper respiratory tract infection
Blood and lymphatic system disorders	Frequent	Anaemia
	Less frequent	Thrombocytopenia,

		leukopenia, neutropenia
Immune system disorders	Less frequent	Hypersensitivity, angioedema, urticaria
Metabolism and nutrition disorders	Frequent	Decrease in or loss of appetite
	Frequency unknown	Diabetes mellitus, hyperglycaemia
Psychiatric disorders	Frequent	Decreased libido, depression
Nervous system disorders	Frequent	Dizziness, somnolence
	Less frequent	Fever, neuromuscular symptoms or neuropathy, confusion, dryness of mouth, nervousness
Cardiac disorders	Frequent	Myocardial infarct (fatal outcomes have been reported), cardiac failure[1]
	Less frequent	Hypertension
	Frequency unknown	Angina, conduction defects including PR and QT interval prolongation, dysrhythmias and non-specific ECG changes
Vascular disorders	Frequent	Hot flushes
Respiratory, thoracic and mediastinal disorders	Less frequent	Interstitial lung disease* (fatal outcomes have been reported), dyspnoea, pulmonary disorder, runny nose, sore throat, tightness in chest
Gastrointestinal disorders	Frequent	Abdominal pain, constipation,

		diarrhoea, nausea, dyspepsia, flatulence
	Less frequent	Gastrointestinal or rectal bleeding, bloated feeling, gas or indigestion, vomiting
	Frequency unknown	Anorexia
Hepato-biliary disorders	Frequent	Hepatotoxicity, jaundice, including cholestatic jaundice, hypertransaminasaemia[1], non-alcoholic fatty liver disease and associated liver diseases
	Less frequent	Hepatitis, methaemoglobinaemia, hepatic failure[*] (fatal outcomes have been reported
Skin and subcutaneous tissue disorders	Frequent	Alopecia, hirsutism/hair re-growth, dry skin, pruritus, rash
	Less frequent	Photosensitivity reaction, itching of skin
	Frequency unknown	Sweating
Renal and urinary disorders	Frequent	Haematuria
	Frequency unknown	Nocturia
Reproductive system and breast disorders	Frequent	Gynaecomastia, breast tenderness, erectile dysfunction
General disorder	Frequent	Weakness (asthenia), oedema, chest pain

	Less frequent	Chills, drowsiness, flu-like syndrome, headache
Investigations	Frequent	Weight increase

*Listed as an adverse drug reaction following review of post-marketing data.

[1.] Hepatic changes are rarely severe and were frequently transient, resolving or improving with continued therapy or following cessation of therapy.

Reporting of suspected adverse reactions:

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

4.9 Overdose:

There is no experience of human overdosage. No specific therapeutic recommendation can be made in cases of overdosage.

Dialysis may not be helpful, since BICALUTAMIDE TEVA is not recovered unchanged in the urine due to its high protein binding.

Frequent monitoring of vital signs and general supportive care is indicated.

5. PHARMACOLOGICAL PROPERTIES:

5.1 Pharmacodynamic properties:

A.21.12 Hormone inhibitors.

ATC code: L02BB03

Mechanism of action:

Bicalutamide is a non-steroidal anti-androgen without any other endocrine activity. It binds to androgen receptors without activating gene expression and thus exhibits androgen stimulation. The inhibition of the androgen stimulus results in the regression of prostatic tumours.

Bicalutamide is a racemate with the (R)-enantiomer exclusively responsible for the anti-androgen activity.

5.2 Pharmacokinetic properties:

Absorption and Distribution:

Bicalutamide is well absorbed after oral administration and is 96 % bound to plasma protein. Food has not proven to significantly affect the extent of bioavailability of bicalutamide.

Biotransformation:

Bicalutamide undergoes extensive metabolism in the liver, the active (R)-enantiomer predominately by oxidation. The half-life of the (R)-enantiomer is about 6 to 7 days, and may be prolonged still further in severe hepatic impairment.

5. PHARMACEUTICAL PARTICULARS:

6.1 List of excipients:

The other ingredients in BICALUTAMIDE TEVA are:

Colloidal silica anhydrous

Croscarmellose sodium

Lactose monohydrate

Magnesium stearate

Microcrystalline cellulose

Opadry OY-GM-28900 white

Povidone

Purified water

Sodium laurilsulfate.

6.2 Incompatibilities:

Not applicable.

6.3 Shelf life:

36 months.

6.4 Special precautions for storage:

Store at or below 25 ºC.

Do not remove blisters from carton until required for use.

KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents of container:

BICALUTAMIDE 50 TEVA tablets are packed into PVC/PVdC (transparent) and Al/PVC/PVdC blister strips in pack sizes of 28 or 30 tablets and the blister strips are packed into a carton.

BICALUTAMIDE 150 TEVA tablets are packed into PVC/PVdC (transparent) and Al/PVC/PVdC blister strips in pack sizes of 28 or 30 tablets and the blister strips are packed into a carton.

6.6 Special precautions for disposal of a used medicine or waste materials derived from such medicine and other handling of the product:

No special requirements.

6. HOLDER OF THE CERTIFICATE OF REGISTRATION:

Teva Pharmaceuticals (Pty) Ltd.

Building 3, Maxwell Office Park

Magwa Crescent West, Waterfall City

Midrand, Gauteng

2090

7. REGISTRATION NUMBER(S):

BICALUTAMIDE 50 TEVA: 43/21.12/0764

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BICALUTAMIDE 150 TEVA: 43/21.12/0765

8. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION:

25 November 2011

9. DATE OF REVISION OF TEXT:

17 December 2024