Teva Pharmaceuticals (Pty) Ltd
Product name: Teva Bicalutamide
Dosage form and strength: Film-coated tablets; 50 mg & 150 mg

PACKAGE INSERT:

SCHEDULING STATUS:

S4

1. NAME OF THE MEDICINE:

TEVA BICALUTAMIDE 50 (Film-coated tablets)

TEVA BICALUTAMIDE 150 (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:

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

TEVA BICALUTAMIDE 150: 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:

TEVA BICALUTAMIDE 50:

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

TEVA BICALUTAMIDE 150:

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

TEVA BICALUTAMIDE 150 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:

TEVA BICALUTAMIDE 50:

Adult males (including the elderly):

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

TEVA BICALUTAMIDE 150:

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:

TEVA BICALUTAMIDE is contraindicated in:

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

4.4 Special warnings and precautions for use:

Since TEVA BICALUTAMIDE 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 TEVA BICALUTAMIDE. Caution should be exercised with the co-administration of TEVA BICALUTAMIDE with medicines metabolised by cytochrome P450 (see **section 4.5**). TEVA BICALUTAMIDE can increase the risk of non-alcoholic fatty liver disease (NAFLD) and associated liver disease.

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

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 TEVA BICALUTAMIDE is initiated in a patient stabilised on a coumarin-derivative anticoagulant. TEVA BICALUTAMIDE may displace coumarin anticoagulants, such as warfarin, from their protein binding sites. Adjustment of anticoagulant dosage may be necessary.

Concurrent administration of TEVA BICALUTAMIDE 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 TEVA BICALUTAMIDE.

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 TEVA BICALUTAMIDE, midazolam exposure (AUC) was increased by up to 80 %, after co-administration with TEVA BICALUTAMIDE 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 TEVA BICALUTAMIDE with compounds such as these, (see **section 4.4**)

4.6 Fertility, pregnancy and lactation:

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

4.7 Effects on ability to drive and use machines:

TEVA BICALUTAMIDE 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,** **jandice, 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 are no experience of human overdosage. No specific therapeutic recommendation can be made in cases of overdosage.

Dialysis may not be helpful, since TEVA BICALUTAMIDE 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 6-7 days, and may be prolonged still further in severe hepatic impairment.

6. PHARMACEUTICAL PARTICULARS:

6.1 List of excipients:

The other ingredients in TEVA BICALUTAMIDE 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:

TEVA BICALUTAMIDE 50 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.

TEVA BICALUTAMIDE 150 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.

7. HOLDER OF THE CERTIFICATE OF REGISTRATION:

Teva Pharmaceuticals (Pty) Ltd.

1st Floor, Building 3, Maxwell Office Park

Magwa Crescent West, Waterfall City

Midrand, Gauteng

2090

8. REGISTRATION NUMBER(S):

TEVA BICALUTAMIDE 50: 43/21.12/0764

TEVA BICALUTAMIDE 150: 43/21.12/0765

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

25 November 2011

10. DATE OF REVISION OF TEXT:

29 April 2023