**PROFESSIONAL INFORMATION**

**SCHEDULING STATUS: S4**

## 1 NAME OF THE MEDICINE

**BICALOX** 50 mg film-coated tablets.

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains:
Bicalutamide 50 mg

Excipients with known effect:
BICALOX tablet contains sugar (lactose).
Each tablet contains 60, 62 mg lactose monohydrate.

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

## 3. PHARMACEUTICAL FORM

**Film coated tablets.**

BICALOX 50 mg is a white to off-white, round, film coated, biconvex tablets, engraved with 'BC 50' on one face and plain on the other.

### 4.1 Therapeutic indications

Treatment of advanced prostate cancer in combination with
luteinizing hormone releasing hormone (LHRH) analogue therapy or surgical castration.

### 4.2 Posology and method of administration

**Posology**

**Adult males including the elderly:**
One tablet (50 mg) once a day. Treatment with Bicalox 50 mg should be started at least three days before commencing treatment with a LHRH analogue, or at the same time as surgical castration.

**Renal Impairment:**

No dosage adjustment is necessary for patients with renal impairment.

**Hepatic Impairment:**

No dosage adjustment is necessary for patients with mild hepatic impairment.

Increased accumulation may occur in patients with moderate to severe hepatic impairment (see section 4.4).

**Paediatric population**

BICALOX 50 mg is contraindicated in children (see section 4.3).

**Method of administration**

Oral use

The tablets should be swallowed whole with liquid.

**4.3 Contraindications**

BICALOX is contraindicated in the following:

- Females and children, pregnant women, or breastfeeding mothers.
- BICALOX 50 mg must not be given to any patient who has known hypersensitivity to bicalutamide or to any of the other excipients.

**4.4 Special warnings and precautions for use**

**Hepatic function impairment:**

**BICALOX 50 mg** is extensively metabolised in the liver. Data suggests that its elimination may be slower in subjects with severe hepatic impairment, and this could lead to increased accumulation of **BICALOX 50 mg.**

Metabolism of **BICALOX 50 mg** may be delayed in patients with moderate to severe hepatic function impairment, resulting in a prolonged elimination half-life and increased risk of toxicity. Therefore, **BICALOX 50 mg** should be used with caution in patients with moderate to severe hepatic impairment.

Periodic liver function testing should be considered during long-term use of **BICALOX 50 mg**, due to the possibility of hepatic changes. The majority of changes are expected to occur within the first 6 months of **BICALOX** therapy.

Severe hepatic changes have been observed infrequently **with BICALOX 50 mg** (see section 4.8). **BICALOX 50 mg** therapy should be discontinued if changes are severe.

**Non-Alcoholic Fatty Liver Disease (NAFLD)**

Testosterone deficiency was associated with higher serum and hepatic levels of triglycerides and higher serum levels of low-density lipoprotein (LDL) in the body, with significant increases in fasting plasma glucose and insulin levels. Patients who receive androgen deprivation therapy (ADT) such as

BICALOX 50 mg are at a greater risk of non-alcoholic fatty liver disease. ADT is associated with significant increase in incidences of other liver diseases such as cirrhosis, liver necrosis, and any liver disease (see section 4.8).

**Medicines metabolised by cytochrome P450:**

Although clinical studies using antipyrine as a marker of Cytochrome P450 (CYP) activity showed no evidence of a drug interaction potential with BICALOX 50 mg, midazolam exposure (AUC) was increased by up to 80 %, after co-administration with BICALOX 50 mg 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 BICALOX 50 mg with compounds such as these.

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

**4.5 Interactions with other medicines and other forms of interaction**

**Luteinising hormone releasing factor (LHRF):**
There is no evidence of any pharmacodynamic or pharmacokinetic interactions between **BICALOX 50 mg** and LHRF analogues.

**Ketoconazole and cimetidine:**
Formal interaction studies have not been undertaken, but caution should be exercised when prescribing **BICALOX 50 mg** with other medicines, e.g., ketoconazole and cimetidine, which may inhibit oxidation of **BICALOX 50 mg**. It could result in increased plasma concentrations of **BICALOX 50 mg** which could lead to an increase in side-effects.

**Coumarin anticoagulants:**
**BICALOX 50 mg** can displace the coumarin anticoagulant, warfarin, from its protein binding sites. It is therefore recommended that if **BICALOX 50 mg** is started in patients, who are already receiving coumarin anticoagulants, prothrombin time should be closely monitored.

**4.6 Fertility, pregnancy, and lactation**
**Pregnancy**
BICALOX is contraindicated in females and must not be given to pregnant women (see section 4.3).

**Breast-feeding**
BICALOX is contraindicated in females and must not be given to nursing mothers (see section 4.3).

**Fertility**
Reversible impairment of male fertility has been observed in animal studies (see section 5.3). A period of subfertility or infertility should be assumed in man.

**4.7 Effects on ability to drive and use machine.**
During treatment with BICALOX, somnolence has been reported and those patients who experience this symptom should not drive or use machines.

**4.8 Undesirable effects**
**Blood and lymphatic system disorders** Frequent: Anaemia
The following side effects have been reported but the frequencies are Unknown:
Leucopenia, neutropenia, thrombocytopenia.

**Immune system disorders**
Less frequent: Hypersensitivity reactions (including angioneurotic oedema and urticaria)

**Metabolism and nutrition disorders** Frequent: Anorexia, decreased appetite.
The following side effects have been reported but the frequencies are unknown: Diabetes mellitus, hyperglycaemia.

**Psychiatric disorders**
Frequent: depression, decreased libido

**Nervous system disorders**
Frequent: Dizziness, somnolence, insomnia

Less frequent: Reversible neurological reactions such as nervousness, drowsiness, and confusion dizziness, insomnia and somnolence.

**Cardiac disorders**
Frequent: Myocardial infarction (fatal outcomes have been reported), cardiac failure

**Vascular disorders**
Frequent: Hypertension, Hot flush

**Respiratory, thoracic, and mediastinal disorders**
Frequent: Upper respiratory tract infection, cough or hoarseness, runny nose, shortness of breath, sore throat, and sneezing
Less frequent: Interstitial lung disease and dyspnoea. Fatal outcomes have been reported.

**Gastrointestinal disorders**
Frequent: Abdominal pain, constipation, nausea, dyspepsia, flatulence, diarrhoea Less frequent: Gastro-intestinal or rectal bleeding, vomiting.

**Hepato-biliary disorders**
Frequent: Hepatic changes (including elevated levels of transaminases, jaundice), hepatitis

Less frequent: Hepatic failure. The following side effects have been reported but the frequencies are unknown: Methaemoglobinaemia, non-alcoholic fatty liver disease (see section 4.4).

**Skin and subcutaneous tissue disorders**

Frequent: Alopecia, hirsuitism/hair re-growth, dry skin, pruritis, rash, sweating

**Renal and urinary disorders** Frequent: Haematuria

The following side effects have been reported but the frequencies are unknown: Nocturia

**Reproductive system and breast disorders**

Frequent: Gynaecomastia and breast tenderness, impotence, decreased libido, erectile dysfunction

**General disorders and administration site conditions**

Frequent: Asthenia, oedema, chest pain, fever, chills, flu-like syndrome

**Investigations** Frequent: Weight gain

***Reporting of suspected adverse reactions***

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 requested to report any suspected adverse reactions to SAHPRA via the Med Safety App (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website. You can also report side effects to Acino Pharma via email on drugsafety_ZA@acino.swiss.

**4.9 Overdose**

There is no human experience of overdosage. There is no specific antidote; treatment should be symptomatic. Dialysis may not be helpful, since Bicalox mg is highly protein bound and is not recovered unchanged in the urine. General supportive care, including frequent monitoring of vital signs, is indicated.

**5. PHARMACOLOGICAL PROPERTIES**

**5.1 Pharmacodynamic properties**

A. 21.12 Hormone inhibitors

Bicalutamide is a non-steroidal anti-androgen, devoid of other endocrine activity. It binds to androgen receptors without activating gene expression, and thus inhibits the androgen stimulus. Regression of prostatic tumours results from this inhibition. Bicalutamide is a racemate with its anti-androgenic activity being almost exclusively in the (R) - enantiomer. Bicalutamide is an anti-androgen and a mixed function oxidase enzyme inducer in animals. Target organ changes, including tumour induction, in animals, are related to these activities. None of the findings in the preclinical testing is considered to have relevance to the treatment of advanced prostate cancer patients.

**5.2 Pharmacokinetic properties**

Bicalutamide is highly plasma protein bound and extensively metabolised (via oxidation and glucuronidation); Its metabolites are eliminated via the kidneys and bile in approximately equal portions.
Distributed into most body tissues.

**5.3 Preclinical safety data**

The toxicological profile of ibuprofen has been established in Animal experiments and in humans from extensive clinical experience. There are no new preclinical data of relevance to the prescriber which are additional to the data already presented in this professional information.

**6 PHARMACEUTICAL PARTICULARS**

**6.1 List of excipients**

The other ingredients are:
Lactose monohydrate, Magnesium stearate Opadry white Povidone K30 Sodium starch glycolate

**6.2 Incompatibilities**

Not applicable.

**6.3 Shelf life**

3 years

**6.4 Special precautions for storage**

Store at or below 30 °C. Store in original package.

**6.5 Nature and contents of container**

BICALOX 50 mg Tablets: 10 tablets per Clear PVC / PVdC-Aluminium blister strip, supplied in a pack size of 30.

**6.6 Special precautions for disposal and other handling**

No special requirements

**7 HOLDER OF CERTIFICATE OF REGISTRATION**

Acino Pharma (Pty) Ltd.
106 16th Road Midrand,
1686

**8 REGISTRATION NUMBER**

41/21.12/0818

**9 DATE OF AUTHORISATION/ RENEWAL OF THE AUTHORISATION**

5 March 2009

**10. DATE OF REVISION OF THE TEXT**

30 September 2024