BICALOX

Bicalox Film-coated tablet 50 mg

douglas

Presentation
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.

Pharmacodynamics
BICALOX 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. Clinically, discontinuation of BICALUTAMIDE can result in antiandrogen withdrawal syndrome in a subset of patients.

BICALOX is a racemate with its antiandrogenic activity being almost exclusively in the R-enantiomer.

Pharmacokinetics
BICALUTAMIDE is well absorbed following oral administration. There is no evidence of any clinically relevant effect of food on bioavailability.

The (S)-enantiomer is rapidly cleared relative to the (R)-enantiomer, the latter having a plasma elimination half-life of about 1 week.

On daily administration of BICALUTAMIDE, the (R)-enantiomer accumulates about 10-fold in plasma as a consequence of its long half-life.

Steady state plasma concentrations of the (R)-enantiomer of approximately 9 µg/mL are observed during daily administration of 50 mg doses of BICALUTAMIDE. At steady state the predominantly active (R)-enantiomer accounts for 99% of the total circulating enantiomers.

The pharmacokinetics of the (R)-enantiomer are unaffected by age, renal impairment or mild to moderate hepatic impairment. There is evidence that for subjects with severe hepatic impairment, the (R)-enantiomer is more slowly eliminated from plasma.

BICALUTAMIDE is highly protein bound (racemate 96%, R-bicalutamide 99.6%) and extensively metabolised (oxidation and glucuronidation); its metabolites are eliminated via the kidneys and bile in approximately equal proportions.

The mean concentration of R-bicalutamide in semen of men receiving 150 mg of bicalutamide was 4.9 µg/mL. The amount of bicalutamide potentially delivered to a female partner during intercourse is low and equates to approximately 0.3 µg/kg. This is below that required to induce changes in offspring of laboratory animals.

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

Recommended Dose

Adult males including the elderly
One tablet (50 mg) once a day.

Treatment with BICALOX should be started at least 3 days before commencing treatment with an LHRH analogue, or at the same time as surgical castration.

Children
BICALOX is contraindicated in children.

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.

Contraindications
BICALOX is contraindicated in females and children.

BICALOX must not be given to any patient who has shown a hypersensitivity reaction to its use.

Warnings and Precautions
BICALOX is extensively metabolised in the liver. On the basis of currently available investigations, there may be slower excretion and accumulation of BICALOX in instances of severe hepatic impairment. Caution is therefore required with patients with moderate to severe hepatic impairment. In these cases regular liver function tests (bilirubin, transaminases, alkaline phosphatase) must be carried out. The majority of changes are expected to occur within the first 6 months of BICALOX therapy.

Severe hepatic changes have been observed rarely with BICALOX. If there is clinical and/or biochemical evidence of severe hepatotoxicity, consideration should be given to discontinue the BICALOX therapy.

Effects on ability to drive and use machines
BICALOX is unlikely to impair the ability of patients to drive or operate machinery. However, it should be noted that occasionally somnolence may occur. Any affected patients should exercise caution.

Side Effects

Table 1 Frequency of Adverse reactions

System Organ Class	Frequency	Event
Blood and lymphatic system disorders	Very common	Anaemia
Immune system disorders	Uncommon	Hypersensitivity, angioedema and urticaria
Metabolism and nutrition disorders	Common	Decreased appetite
Psychiatric disorders	Common	Decreased libido, depression
Nervous system disorders	Very common	Dizziness
	Common	Somnolence
Cardiac disorders	Common	Myocardial infarction, Cardiac failure
Vascular disorders	Very common	Hot flush
Respiratory, thoracic and mediastinal disorders	Uncommon	Interstitial lung disease
Gastrointestinal disorders	Very common	Abdominal pain, constipation, nausea
	Common	Dyspepsia, flatulence
Hepato-biliary disorders	Common	Hepatotoxicity, jaundice, Hypertransaminasaemia
	Rare	Hepatic failure
Skin and subcutaneous tissue disorders	Common	Alopecia, hirsutism/hair re-growth, dry skin, pruritus rash
Renal and urinary disorders	Very common	Haematuria
Reproductive system and breast disorders	Very Common	Gynaecomastia and breast tenderness
	Common	Erectile Dysfunction
General disorders and administration site conditions	Very common	Asthenia, oedema
	Common	Chest pain
Investigations	Common	Weight increased

Printed: Black
Size: 297 x 210 mm
File Name: 302330 Bicalox 50mg
Date: Thursday 18 June, 2015

Interactions with other medicaments

There is no evidence of any pharmacodynamic or pharmacokinetic interactions between BICALUTAMIDE and LHRH analogues.

In vitro studies have shown that R-bicalutamide is an inhibitor of CYP 3A4, with lesser inhibitory effects on CYP 2C9, 2C19 and 2D6 activity.

Although clinical studies using antipyrine as a marker of cytochrome P450 (CYP) activity showed no evidence of a drug interaction potential with BICALUTAMIDE, mean midazolam exposure (AUC) was increased by up to 80%, after co-administration of BICALUTAMIDE for 28 days. For drugs with a narrow therapeutic index such an increase could be of relevance. As such, concomitant use of terfenadine, astemizole and cisapride is contraindicated. Caution should be exercised with the co-administration of BICALUTAMIDE with compounds such as ciclosporin and calcium channel blockers. Dosage reduction may be required for these drugs particularly if there is evidence of enhanced or adverse drug effect. For ciclosporin, it is recommended that plasma concentrations and clinical condition are closely monitored following initiation or cessation of BICALUTAMIDE therapy.

Caution should be exercised when prescribing BICALUTAMIDE with other drugs which may inhibit drug oxidation e.g. cimetidine and ketoconazole. In theory, this could result in increased plasma concentrations of BICALUTAMIDE which theoretically could lead to an increase in side effects.

In vitro studies have shown that BICALUTAMIDE can displace the coumarin anticoagulant, warfarin, from its protein binding sites. It is therefore recommended that if BICALUTAMIDE is started in patients who are already receiving coumarin anticoagulants, prothrombin time should be closely monitored.

Pregnancy and Lactation

BICALOX is contraindicated in females and must not be given to pregnant women or nursing mothers.

Symptons and treatment of overdose

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

Pharmaceutical Precautions

Instructions for Use/Handling
No special precautions required.

Incompatibilities
None known.

Shelf Life
36 Months

Special Precautions for Storage
Store below 30°C, protect from light and moisture.

Medicine Classification

Prescription Medicine.

Package Quantity

Carton of blisters containing 28 tablets.

Further Information

List of Excipients
- Lactose
- Sodium Starch Glycollate
- Povidone
- Magnesium Stearate
- Opadry White Y-1-7000

Name and Address of Product Owner

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Date of preparation May 2015

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