141.0 mm

BITAMID 50mg Tablet
(Bicalutamide)

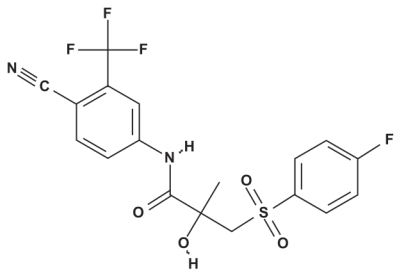
بیٹامیڈ ۵۰ ملی گرام ٹیبلٹ
(بائی کیلوٹامائیڈ)

206.0 mm

COMPOSITION
Bitamid Tablet 50mg
Each film coated tablet contains:
Bicalutamide.....50mg
(USP Specifications)

DESCRIPTION
The active component of BITAMID is bicalutamide. Bicalutamide is a non-steroidal androgen receptor inhibitor with no other known endocrine activity. The chemical name is propanamide, N-[4-cyano-3-(trifluoromethyl) phenyl]-3-[(4-fluorophenyl) sulfonyl]-2-hydroxy-2-methyl,(+-).
Bicalutamide is an antineoplastic hormonal agent primarily used in the treatment of prostate cancer. Bicalutamide is a pure, nonsteroidal anti-androgen with affinity for androgen receptors (but not for progestogen, estrogen, or glucocorticoid receptors).

MOLECULAR & STRUCTURAL FORMULA
Molecular formula of Bicalutamide is as follows:
$C_{18}H_{14}F_4N_2O_4S$
Structural formula of Bicalutamide is as follows:



CLINICAL PHARMACOLOGY
MODE OF ACTION
BITAMID (bicalutamide) is a non-steroidal androgen receptor inhibitor. It competitively inhibits the action of androgens by binding to cytosol androgen receptors in the target tissue. Prostatic carcinoma is known to be androgen sensitive and responds to treatment that counteracts the effect of androgen and/or removes the source of androgen.
When BITAMID (bicalutamide) is combined with luteinizing hormone releasing hormone (LHRH) analogue therapy, the suppression of serum testosterone induced by the LHRH analogue is not affected. However, in clinical trials with BITAMID (bicalutamide) as a single agent for prostate cancer, rises in serum testosterone and estradiol have been noted.
In a subset of patients who have been treated with BITAMID (bicalutamide) and an LHRH agonist, and who discontinue BITAMID (bicalutamide) therapy due to progressive advanced prostate cancer, a reduction in Prostate Specific Agent (PSA) and/or clinical improvement (antiandrogen withdrawal phenomenon) may be observed.

INDICATIONS
BITAMID (bicalutamide) 50 mg daily is indicated for use in combination therapy with a luteinizing hormone-releasing hormone (LHRH) analog for the treatment of Stage D2 metastatic carcinoma of the prostate.

DOSAGE & ADMINISTRATION
The recommended dose for BITAMID (bicalutamide) therapy in combination with an LHRH analogue is one 50 mg tablet once daily (morning or evening), with or without food. It is recommended that BITAMID (bicalutamide) be taken at the same time each day. Treatment with BITAMID (bicalutamide) should be started at the same time as treatment with an LHRH analogue.
Dosage Adjustment in Renal Impairment
No dosage adjustment is necessary for patients with renal impairment.

Dosage Adjustment in Hepatic Impairment
No dosage adjustment is necessary for patients with mild to moderate hepatic impairment. In patients with severe liver impairment (n=4), although there was a 76% increase in the half-life (5.9 and 10.4 days for normal and impaired patients, respectively) of the active enantiomer of bicalutamide no dosage adjustment is necessary

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 9µg/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 the (R)-enantiomer is more slowly eliminated from plasma in patients with severe hepatic impairment.
Bicalutamide is highly protein bound (racemate 96%, (R)-enantiomer >99.6%) and extensively metabolised (via oxidation and glucuronidation). Its metabolites are eliminated via the kidneys and bile in approximately equal proportions.
In a clinical study the mean concentration of (R)-bicalutamide in semen of men receiving bicalutamide 150 mg was 4.9 µg/ml. The amount of bicalutamide potentially delivered to a female partner during intercourse is low and by extrapolation possibly equates to approximately 0.3 µg/kg. This is below that required to induce changes in offspring of laboratory animals.

PRECAUTIONS
Hepatitis
Rare cases of death or hospitalization due to severe liver injury have been reported post-marketing in association with the use of BITAMID (bicalutamide). Hepatotoxicity in these reports generally occurred within the first three to four months of treatment. Hepatitis or marked increases in liver enzymes leading to drug discontinuation occurred in approximately 1% of BITAMID (bicalutamide) patients in controlled clinical trials.
Serum transaminase levels should be measured prior to starting treatment with BITAMID (bicalutamide), at regular intervals for the first four months of treatment, and periodically thereafter. If clinical symptoms or signs suggestive of liver dysfunction occur (e.g., nausea, vomiting, pain, fatigue, anorexia, "flu-like" symptoms, dark urine, jaundice, or right upper quadrant tenderness), the serum transaminases, in particular the serum ALT, should be measured immediately. If at any time a patient has jaundice, or their ALT rises above two times the upper limit of normal, BITAMID (bicalutamide) should be immediately discontinued with close follow-up of liver function.

Gynecomastia and Breast Pain
In clinical trials with BITAMID (bicalutamide) 150 mg as a single agent for prostate cnacer, gynecomastia and breast pain have been reported in up to 38% and 39% of patients, respectively.

Glucose Tolerance
A reduction in glucose tolerance has been observed in males receiving LHRH agonists. This may manifest as diabetes or loss of glycemic control in those with pre-existing diabetes. Consideration should therefore be given to monitoring blood glucose in patients receiving BITAMID (bicalutamide) in combination with LHRH agonists.

Laboratory Tests
Regular assessments of serum Prostate Specific Antigen (PSA) may be helpful in monitoring the patient's response. If PSA levels rise during BITAMID (bicalutamide) therapy, the patient should be evaluated for clinical progression. For patients who have objective progression of disease together with an elevated PSA, a treatment-free period of antiandrogen, while continuing the LHRH analogue, may be considered.

Pregnancy
Pregnancy Category X
Based on its mechanism of action, BITAMID (bicalutamide) may cause fetal harm when administered to a pregnant woman. BITAMID (bicalutamide) is contraindicated in women, including those who are or may become pregnant. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to a fetus.
Nursing Mothers
BITAMID (bicalutamide) is not indicated for use in women.
Adverse Reactions
Body as a Whole:
Neoplasm; Neck Pain; Fever; Chills; Sepsis; Hernia; Cyst
Cardiovascular:
Angina Pectoris; Congestive Heart Failure; Myocardial Infarct; Heart Arrest; Coronary Artery Disorder; Syncope
Digestive:
Melena; Rectal Haemorrhage; Dry Mouth; Dysphagia; Gastrointestinal Disorder; Periodontal Abscess; Gastrointestinal Carcinoma
Metabolic and Nutritional:
Edema; BUN Increased; Creatinine Increased, Dehydration; Gout; Hypocholesteremia
Musculoskeletal:
Myalgia; Leg Cramps
Nervous:
Hypertonia; Confusion; Somnolence; Libido Decreased; Neuropathy; Nervousness
Respiratory:
Lung Disorder; Asthma; Epistaxis; Sinusitis
Skin and Appendages:
Dry Skin; Alopecia; Pruritus; Herpes Zoster; Skin Carcinoma; Skin Disorder
Special Senses:
Cataract specified
Urogenital:
Dysuria; Urinary Urgency; Hydronephrosis; Urinary Tract Disorder
Abnormal Laboratory Test Values:
Laboratory abnormalities including elevated AST, ALT, bilirubin, BUN, and creatinine and decreased haemoglobin and white cell count have been reported in both BITAMID (bicalutamide) -LHRH analogue treated and flutamide-LHRH analogue treated patients

DRUG INTERACTIONS
Clinical studies have not shown any drug interactions between bicalutamide and LHRH analogs (goserelin or leuprolide). There is no evidence that bicalutamide induces hepatic enzymes.
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. Clinical studies have shown that with co-administration of BITAMID (bicalutamide), mean midazolam (a CYP 3A4 substrate) levels may be increased 1.5 fold (for Cmax) and 1.9 fold (for AUC). Hence, caution should be exercised when BITAMID (bicalutamide) is co-administered with CYP 3A4 substrates.
In vitro protein-binding studies have shown that bicalutamide can displace coumarin anticoagulants from binding sites. Prothrombin times should be closely monitored in patients already receiving coumarin anticoagulants who are started on BITAMID (bicalutamide) and adjustment of the anticoagulant dose may be necessary.

CONTRAINDICATIONS
- Hypersensitivity to the active substance or to any of the excipients.
- Bicalutamide is contraindicated in pregnant women, lactating mothers and children.
- Co-administration of terfenadine, astemizole or cisapride with bicalutamide is contraindicated.

STORAGE & INSTRUCTIONS:
Store between 20-25°C. Protect from sunlight, heat and moisture.
Keep away from the reach of children.
To be sold on the prescription of a registered oncologist or on demand from cancer hospitals, institutions and oncologists only.

HOW SUPPLIED
Bitamid Tablet 50mg:
10's, 28's film coated tablets

206.0 mm

خوراک وطریقہ استعمال:
سرطان کے ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

ہدایات:
دوا کو ۲۰-۲۵ ڈگری سینٹی گریڈ درجہ حرارت کے درمیان رکھیں۔
دھوپ، گرمی اور نمی سے محفوظ رکھیں۔
بچوں کی پہنچ سے دور رکھیں۔
صرف مستند اونکولوجسٹ یا کینسر ہسپتال کے نسخے پر فروخت کریں۔

Manufactured by:
PHARMASOL
PRIVATE LIMITED
Plot # 549,Sundar Industrial Estate,
Lahore, Pakistan.