



Get medical help right away, if you have:

- trouble breathing with or without a cough or fever. Some people who take bicalutamide may get an inflammation in the lungs called mediastinal lung disease.
- a change in urination. Symptoms of an allergic reaction include: itching of the face, swelling of the lips, tongue, throat or trouble swallowing.
- dizziness of the ear and eye pain (darkness), dizziness, dark urine, right upper stomach body pain. These may be symptoms of liver damage.
- loss of appetite, constipation, or trouble sleeping.
- pain in your chest, arms, legs, or joints.
- changes in your vision, such as double vision, blurred vision, or spots.
- changes in your urine.
- weakness from being unable to sit right.
- feeling dizzy.
- feeling very hot or cold (chills/fever).

**What are the possible side effects of bicalutamide?**  
 There are not all the possible side effects of bicalutamide. For more information, ask your healthcare provider or pharmacist.

**HOW SHOULD I STORE BICALUTAMIDE TABLETS 50 mg?**  
 Store bicalutamide tablets 50 mg in their original container. Do not use bicalutamide tablets if the container is torn, the seal is broken, or the tablets are discolored, broken, or missing.

**General information about the safe and effective use of bicalutamide tablets 50 mg.**  
 Bicalutamide tablets 50 mg are prescription only. They should be used only as directed. Do not use bicalutamide tablets 50 mg for a condition for which it was not prescribed. Do not give bicalutamide tablets 50 mg to anyone else, even if they seem to have the same symptoms as you have.

**What are the ingredients in bicalutamide tablets 50 mg?**  
 The active ingredients include: active moieties: bicalutamide, magnesium stearate, hypromellose E5, polyethylene glycol 400, povidone K-30, sodium starch glycolate.

**Manufactured By:**  
 AstraZeneca Pharmaceuticals LP, 4000 State Road, Evansville, IN 47615, USA, NDC 27703-1004, 10 1531 1 017243 issued June 2020

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**11. DESCRIPTION**  
 Tablets contain 50 mg of bicalutamide, a non-steroidal androgen receptor inhibitor with no other known endocrine activity. The chemical name is propanamide, N-[4-(cyano-3-(difluoromethyl)phenyl)-3-((4-fluorophenyl)sulfonyl)-2-hydroxy-2-methyl-1-)]. The structural and empirical formulas are:

CC(C)(O)C1=CC=C(C=C1)S(=O)(=O)C2=CC=C(C=C2)C3=CC=C(C=C3)C#N

**12. CLINICAL PHARMACOLOGY**  
**12.1. Mechanism of Action**  
 Bicalutamide is a non-steroidal androgen receptor inhibitor. It competitively inhibits the action of androgens by binding to cytosolic androgen receptors. Prostate 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 bicalutamide is combined with luteinizing hormone releasing hormone (LHRH) analog therapy, the suppression of serum testosterone induced by the LHRH analog is not affected. However, in clinical trials with 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 bicalutamide and an LHRH agonist, and who discontinue bicalutamide therapy due to progressive advanced prostate cancer, a reduction in Prostate-Specific Antigen (PSA) and/or clinical improvement (and/or withdrawal phenomenon) may be observed.

**12.2. Pharmacokinetics**  
**Absorption**  
 Bicalutamide is well-absorbed following oral administration, although the absolute bioavailability is unknown. Co-administration of bicalutamide with food has no clinically significant effect on rate or extent of absorption. Distribution  
 Bicalutamide is highly protein-bound (86%) [see Drug Interactions (7)]. Metabolism/Excretion  
 Bicalutamide undergoes stereospecific metabolism. The S (inactive) isomer is metabolized primarily by glucuronidation. The R (active) isomer also undergoes glucuronidation but is predominantly oxidized to an inactive metabolite followed by glucuronidation. Both the parent and metabolite glucuronides are eliminated in the urine and feces. The S-enantiomer is rapidly cleared relative to the R-enantiomer, with the R-enantiomer accounting for about 99% of total steady-state plasma levels. Pharmacokinetics of the active enantiomer of bicalutamide in normal males and patients with prostate cancer are presented in Table 2.

**13. NONCLINICAL TOXICOLOGY**  
**13.1. Carcinogenesis, Mutagenesis, Impairment of Fertility**  
 Two-year oral carcinogenicity studies were conducted in both male and female rats and mice at doses of 5, 15 or 75 mg/kg/day of bicalutamide. A variety of tumor target organ effects were identified and were attributed to the androgenicity of bicalutamide. In the rat, the incidence of hepatocellular carcinoma in male mice given 75 mg/kg/day of bicalutamide (approximately 4 times human therapeutic concentrations) and an increased incidence of benign thyroid follicular cell adenomas in rats given 5 mg/kg/day (approximately 2/3 human therapeutic concentrations) and above were recorded. These neoplastic changes were progressive and non-neoplastic changes related to hepatic enzyme induction observed in animal toxicity studies. Enzyme induction has not been observed following bicalutamide administration in man. There were no tumorigenic effects suggestive of genotoxic carcinogenesis. A comprehensive battery of both *in vivo* and *in vitro* genotoxicity tests (yeast gene conversion, Ames, E. coli, CHO/KGPR1, human lymphocyte cytogenetic, mouse micronucleus, and rat bone marrow cytogenetic tests) has demonstrated that bicalutamide does not have genotoxic activity.

Parameter	Mean	Standard Deviation
Normal Males (n=30)		
Apparent Oral Clearance (L/hr)	0.320	0.103
Single Dose Peak Concentration (µg/mL)	0.768	0.178
Single Dose Time to Peak Concentration (hours)	3.1	14.8
Half-life (days)	5.8	2.29
Patients with Prostate Cancer (n=40)		
C <sub>0</sub> (µg/mL)	8.939	3.504

**14. CLINICAL PHARMACOLOGY**  
**14.1. Carcinogenesis, Mutagenesis, Impairment of Fertility**  
 In male rats dosed at 250 mg/kg/day (approximately 2 times human therapeutic concentrations), the precocial interval and time to successful mating were increased in the first pairing but no effects on fertility following successful mating were observed. These effects were reversed by the end of an 11-week period of dosing. No effects on female rats dosed at 10, 50 and 250 mg/kg/day (approximately 2/3, 1 and 2 times human therapeutic concentrations, respectively) or their female offspring were observed. Administration of bicalutamide to pregnant females resulted in feminization of the male offspring leading to hypospadias at all dose levels. Affected male offspring were also infertile. Based on a maximum dose of 50 mg/kg/day of bicalutamide for an average 70 kg patient.

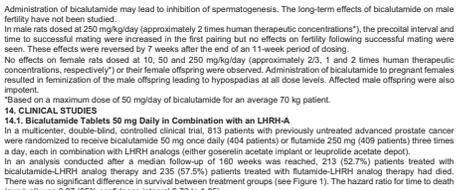
**14.2. CLINICAL STUDIES**  
**14.1. Bicalutamide Tablets 50 mg Daily in Combination with an LHRH-A**  
 In a multicenter, double-blind, controlled clinical trial, 813 patients with previously untreated advanced prostate cancer were randomized to receive bicalutamide 50 mg once daily (404 patients) or flutamide 250 mg (409 patients) three times a day, each in combination with LHRH analogs (either goserelin acetate implant or leuprolide acetate depot). In an analysis conducted after a median follow-up of 160 weeks was reached, 213 (52.7%) patients treated with bicalutamide-LHRH analog therapy and 235 (57.5%) patients treated with flutamide-LHRH analog therapy had died. There was no significant difference in survival between treatment groups (see Figure 1). The hazard ratio for time to death (survival) was 0.87 (95% confidence interval: 0.72 to 1.05).


Figure 1 - The Kaplan-Meier probability of death for both androgen treatment groups.

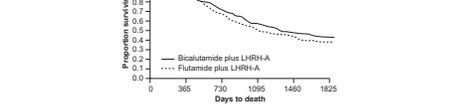


Figure 2 - Kaplan-Meier curve for time to progression for both androgen treatment groups.

**14.2 Safety Data from Clinical Studies using Bicalutamide Tablets 150 mg**  
 Bicalutamide Tablets 150 mg is not approved for use either alone or with other treatments. Two identical multicenter, randomized, open-label trials comparing bicalutamide 150 mg daily monotherapy to castration were conducted in patients that had locally advanced (T3-4, NX, MO) or metastatic (M1) prostate cancer. Monotherapy – M1 Group  
 Bicalutamide 150 mg daily is not approved for use in patients with M1 cancer of the prostate. Based on an interim analysis of the two trials for survival, the Data Safety Monitoring Board recommended that bicalutamide treatment be discontinued in the M1 patients because the risk of death was 25% (HR: 1.25, 95% CI 0.77 to 1.81) and 31% (HR: 1.31, 95% CI 0.97 to 1.77) higher in the bicalutamide treated group compared to that in the castrated group, respectively. Bicalutamide 150 mg daily is not approved for use in patients with locally advanced (T3-4, NX, MO) cancer of the prostate. Following discontinuation of all M1 patients, the trials continued with the T3-4, NX, MO patients until study completion. In the larger trial (N=552), the risk of death was 25% (HR: 1.25, 95% CI 0.92 to 1.71) higher in the bicalutamide group and in the smaller trial (N=140), the risk of death was 36% (HR: 0.64, 95% CI: 0.39 to 1.03) lower in the bicalutamide group. In addition to the above two studies, there are three other on-going clinical studies that provide additional safety information for bicalutamide 150 mg, a dose that is not approved for use. These are three multicenter, randomized, double-blind, parallel group trials comparing bicalutamide 150 mg daily monotherapy (adjunct to previous therapy or under watchful waiting) with placebo, for death or time to disease progression, in a population of 8113 patients with localized or locally advanced prostate cancer. Bicalutamide 150 mg daily is not approved for use as therapy for patients with localized prostate cancer who are candidates for watchful waiting. Data from a planned subgroup analysis of two of these trials in 1627 patients with localized prostate cancer who were under watchful waiting, revealed a trend toward decreased survival in the bicalutamide arm after a median follow-up of 7.4 years. There were 294 (37.7%) deaths in the bicalutamide treated patients versus 270 (32.9%) deaths in the placebo treated patients (localized watchful waiting group) for a hazard ratio of 1.16 (95% CI 0.99 to 1.37).

**16. HOW SUPPLIED/STORAGE AND HANDLING**  
**Bicalutamide Tablets 50 mg**  
 White to off-white, round, biconvex, film coated tablets, debossed 'B 50' on one side and plain on other side.  
 Bottles of 30 Tablets (NDC 16729-023-10)  
 Bottles of 100 Tablets (NDC 16729-023-011)  
**16.1. Storage and Handling**  
 Store at 20° to 25° (68° to 77°F) [see USP Controlled Room Temperature].  
**17. PATIENT COUNSELING INFORMATION**  
 Patients should be informed that therapy with bicalutamide and the LHRH analog should be started at the same time and that they should not interrupt or stop taking these medications without consulting their physician. During treatment with bicalutamide, somnolence has been reported, and those patients who experience this symptom should observe caution when driving or operating machines. Patients should be informed that diabetes, or loss of glycemic control in patients with pre-existing diabetes has been reported during treatment with LHRH agonists. Consideration should therefore be given to monitoring blood glucose in patients receiving bicalutamide in combination with LHRH agonists.

**Manufactured For:**  
 Accord Healthcare, Inc., 5005 State Road, Suite 210-B, Durham, NC 27703, USA.

**Manufactured By:**  
 Intra Pharmaceuticals Limited, Plot No.: 457, 458, Village-Matoda, Bavla Road, Ta. Sanand, Dist. - Anand-382-320, India.

10 1531 1 017243  
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Back Size : 450 x 320 (mm)  
 Colour : Pan Black