SUMMARY OF PRODUCT CHARECTERISTICS OF

BIKATAB (BICALUTAMIDE TABLETS BP 50mg)

1. Name of the medicinal product:

Bikatab (Bicalutamide Tablets BP 50mg)

2. Qualitative and quantitative composition

Each film-coated tablet contains:

Bicalutamide BP 50 mg

Sr. No.	Ingredients	Specification	Qty / Tablet (mg)	Purpose of use
	Dry mixing:			
1.	Bicalutamide	BP	50.000	Active
2.	Lactose Monohydrate**(200#)	BP	62.700	Binder
3.	Povidone (K-25)	BP	5.000	Binder
4.	Sodium Starch Glycolate (Type A)	BP	3.750	Disintegrant
	Granulating vehicle:			
5.	Purified Water #	USP	15.000	Aqueous Solvent
	Pre-Lubrication:			
6.	Sodium Starch Glycolate (Type A)	BP	3.750	Disintegrant
	Lubrication:			
7.	Magnesium Stearate	BP	1.500	Lubricant
Total Uncoated tablet weight:			**126.700**	
	Coating: $			
8.	Opadry OY-S-9622 White	IHS	3.000	Coating agent
9.	Purified Water #	USP	37.500	Aqueous Solvent
Total coated tablet weight			**129.700**	

Note:

Actual quantity of Bicalutamide BP to be dispensed is based on actual % purity of Bicalutamide from the Batch formula worksheet as per subsequent calculation.

** Quantity of Lactose Monohydrate ** BP should adjust to the target weight the calculation shown in the Batch formula Worksheet.

Not present in finished Product.

$ 10% overages included to compensate process loss on coating.

3. Pharmaceutical form

Film-coated tablet.

White, round, biconvex Film coated tablets

4. Clinical particular

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 Bicalutamide should be started at least 3 days before commencing treatment with an 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

Paediatric population: Bicalutamide is contraindicated for use in children

4.3 Contraindications

Bicalutamide is contraindicated in females and children

Hypersensitivity to the active substance or to any of the excipients

Co-administration of terfenadine, astemizole or cisapride with Bicalutamide is contraindicated.

SUMMARY OF PRODUCT CHARECTERISTICS OF

BIKATAB (BICALUTAMIDE TABLETS BP 50mg)

4.4 Special warnings and precautions for use

Initiation of treatment should be under the direct supervision of a specialist.

Bicalutamide is extensively metabolized 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 Bicalutamide. Therefore, Bicalutamide should be used with caution in patients with moderate to severe hepatic impairment. Periodic liver function testing should be considered due to the possibility of hepatic changes. The majority of changes are expected to occur within the first 6 months of Bicalutamide therapy.Severe hepatic changes and hepatic failure have been observed rarely with Bicalutamide, and fatal outcomes have been reported. Bicalutamide therapy should be discontinued if changes are severe.

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

Bicalutamide has been shown to inhibit cytochrome P450 (CYP3A4), as such caution should be exercised when co-administered with drugs metabolised predominantly by CYP3A4 .Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Androgen deprivation therapy may prolong the QT interval.

In patients with a history of or risk factors for QT prolongation and in patients receiving concomitant medicinal products that might prolong the QT interval physicians should assess the benefit risk ratio including the potential for Torsade de pointes prior to initiating Casodex.

Antiandrogen therapy may cause morphological changes in spermatozoa. Although the effect of bicalutamide on sperm morphology has not been evaluated and no such changes have been

reported for patients who received Casodex, patients and/or their partners should follow adequate contraception during and for 130 days after Casodex therapy.

Potentiation of coumarin anticoagulant effects have been reported in patients receiving concomitant Casodex therapy, which may result in increased Prothrombin Time (PT) and International Normalised Ratio (INR). Some cases have been associated with risk of bleeding. Close monitoring of PT/INR is advised and anticoagulant dose adjustment should be considered.

4.5 Interaction with other medicinal products and other forms of interaction

Effects of esomeprazole on the pharmacokinetics of other medicinal products

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 and 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. There have been reports of increased effect of warfarin and other coumarin anticoagulants when co-administered with Bicalutamide. It is therefore recommended that if Bicalutamide is administered in patients who are concomitantly receiving coumarin anticoagulants, PT/INR should be closely monitored and adjustments of anticoagulant dose considered.

Since androgen deprivation treatment may prolong the QT interval, the concomitant use of Bicalutamide with medicinal products known to prolong the QT interval or medicinal products able to induce Torsade de pointes such as class IA (e.g. quinidine, disopyramide) or class III (e.g. amiodarone, sotalol, dofetilide, ibutilide) antiarrhythmic medicinal products, methadone, moxifloxacin, antipsychotics, etc. should be carefully evaluated .

Paediatric population

Interaction studies have only been performed in adults.

4.6 Fertility, pregnancy and lactation
Pregnancy

Bicalutamide is contraindicated in females and must not be given to pregnant women.

Breast-feeding

Bicalutamide is contraindicated during breast-feeding.

Fertility

Reversible impairment of male fertility has been observed in animal studies. A period of subfertility or infertility should be assumed in man.

4.7 Effects on ability to drive and use machines

Bicalutamide 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.

4.8 Undesirable effects

In this section, undesirable effects are defined as follows: Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to ≤1/100); rare (≥1/10,000 to ≤1/1,000); very rare (≤1/10,000); not known (cannot be estimated from the available data).

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 (fatal outcomes have been reported)4, cardiac failure4
	Not known	QT prolongation
Vascular disorders	Very common	Hot flush
Respiratory, thoracic and	Uncommon	Interstitial lung disease5 (fatal

mediastinal disorders		outcomes have been reported).
Gastrointestinal disorders	Very common	Abdominal pain, constipation nausea
	Common	Dyspepsia , flatulence
Hepatobiliary disorders	Common	Hepatotoxicity, jaundice, hypertransaminasaemia1
	Rare	Hepatic failure2 (fatal outcomes have been reported).
Skin and subcutaneous tissue disorders	Common	Alopecia, hirsutism/hair re-growth dry skin, pruritus, rash
	Rare	Photosensitivity reaction
Renal and urinary disorders	Very common	Haematuria
Reproductive system and breast disorders	Very common	Gynaecomastia and breast tenderness3
	Common	Erectile dysfunction
General disorders and administration site conditions	Very common	Asthenia oedema
	Common	Chest pain
Investigations	Common	Weight increased

1. Hepatic changes are rarely severe and were frequently transient, resolving or improving with continued therapy or following cessation of therapy.

2. Listed as an adverse drug reaction following review of post-marketed data. Frequency has been determined from the incidence of reported adverse events of hepatic failure in patients receiving treatment in the open-label Casodex arm of the 150 mg EPC studies.

3. May be reduced by concomitant castration.

4. Observed in a pharmaco-epidemiology study of LHRH agonists and anti-androgens used in the treatment of prostate cancer. The risk appeared to be increased when Casodex 50 mg was used in combination with LHRH agonists, but no increase in risk was evident when Casodex 150 mg was used as a monotherapy to treat prostate cancer.

5. Listed as an adverse drug reaction following review of post-marketed data. Frequency has been determined from the incidence of reported adverse events of interstitial pneumonia in the randomised treatment period of the 150 mg EPC studies.

Increased PT/INR: Accounts of coumarin anticoagulants interacting with Casodex have been reported in post marketing surveillance

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.

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 Bicalutamide 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

Pharmacotherapeutic group: Anti-androgens

ATC code: L02BB03

Mechanism of action

Bicalutamide is a non-steroidal ant 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.Bicalutamide is a racemate with its ant androgenic activity being almost exclusively in the (R)-enantiomer.

5.2 Pharmacokinetic properties

Absorption

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

Distribution

Bicalutamide is highly protein bound (racemate 96% (R)-enantiomer >99%) and extensively metabolised (via oxidation and glucuronidation): Its metabolites are eliminated via the kidneys and bile in approximately equal proportions.

Biotranformation

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 microgram/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.

Elimination

In a clinical study the mean concentration of R-bicalutamide in semen of men receiving Bicalutamide 150 mg was 4.9 microgram/ml. The amount of bicalutamide potentially delivered to a female partner during intercourse is low and by extrapolation possibly equates to approximately 0.3 microgram/kg. This is below that required to induce changes in offspring of laboratory animals.

Special Populations

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 eliminate

6. Pharmaceutical particulars

6.1 List of excipients

Lactose Monohydrate** BP (200#)

Povidone BP (K-25)

Sodium Starch Glycolate BP (Type A)

Sodium Starch Glycolate BP (Type A)

Magnesium Stearate BP

Opadry OY-S-9622 White IHS

6.2 Incompatibilities Not applicable.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Store below 30°C in the original package in order to protect from moisture.

6.5 Nature and contents of container

Clear PVC-Alu blister pack:

2 x 14 Tablets

6.6 Special precautions for disposal and other handling

No special requirements.

SUMMARY OF PRODUCT CHARECTERISTICS OF

BIKATAB (BICALUTAMIDE TABLETS BP 50mg)

7. Marketing authorisation holder

ANNYGOD PHARMA. CO. LTD
D271 OFUOBI LINE,

BRIDGE HEAD MARKET,

ONITSHA, ANAMBRA STATE

NIGERIA.

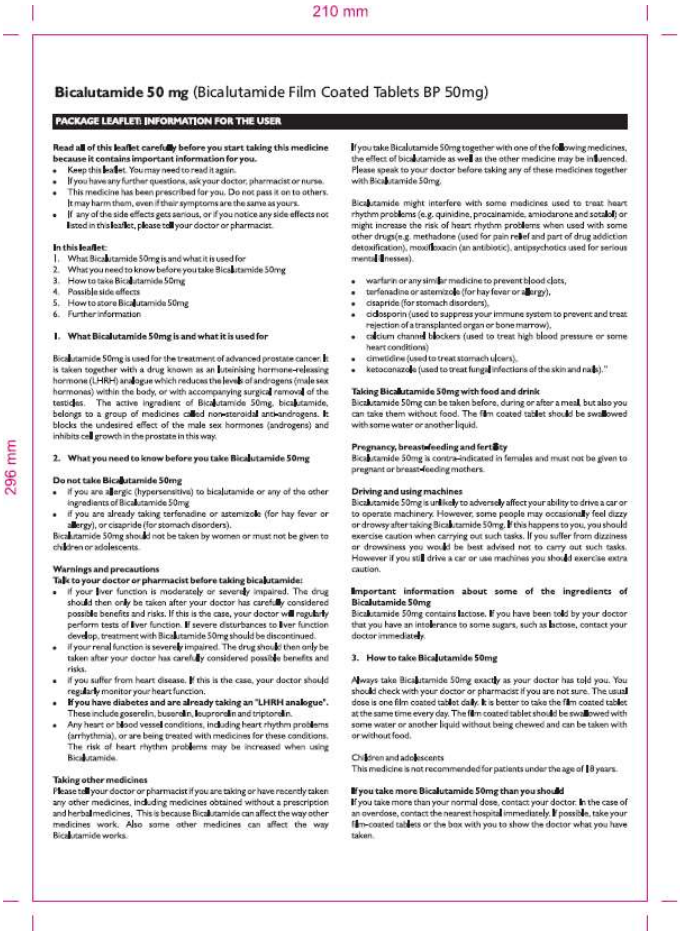
8. Marketing authorisation number(s): NA

9. Date of first authorisation/renewal of the authorisation: NA

10. Date of revision of the text

1.3.3 Package Insert (also known as patient Information PIL)

Enclosed



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Bicalutamide 50 mg (Bicalutamide Film Coated Tablets BP 50mg)

PACKAGE LEAFLET: INFORMATION FOR THE USER

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What Bicalutamide 50mg is and what it is used for

Bicalutamide 50mg is used for the treatment of advanced prostate cancer. It is taken together with a drug known as an luteinising hormone-releasing hormone (LHRH) analogue which reduces the levels of androgens (male sex hormones) within the body, or with accompanying surgical removal of the testicles. The active ingredient of Bicalutamide 50mg, bicalutamide, belongs to a group of medicines called non-steroidal anti-androgens. It blocks the undesired effect of the male sex hormones (androgens) and inhibits cell growth in the prostate in this way.

2. What you need to know before you take Bicalutamide 50mg

Do not take Bicalutamide 50mg
- if you are allergic (hypersensitive) to bicalutamide or any of the other ingredients of Bicalutamide 50mg
- if you are already taking terfenadine or astemizole (for hay fever or allergy), or cisapride (for stomach disorders).

Bicalutamide 50mg should not be taken by women or must not be given to children or adolescents.

Warnings and precautions
Talk to your doctor or pharmacist before taking bicalutamide:
- if your liver function is moderately or severely impaired. The drug should then only be taken after your doctor has carefully considered possible benefits and risks. If this is the case, your doctor will regularly perform tests of liver function. If severe disturbances to liver function develop, treatment with Bicalutamide 50mg should be discontinued.
- if your renal function is severely impaired. The drug should then only be taken after your doctor has carefully considered possible benefits and risks.
- if you suffer from heart disease. If this is the case, your doctor should regularly monitor your heart function.
- **If you have diabetes and are already taking an "LHRH analogue".** These include goserelin, buserelin, leuprorelin and triptorelin.
- Any heart or blood vessel conditions, including heart rhythm problems (arrhythmia), or are being treated with medicines for these conditions. The risk of heart rhythm problems may be increased when using Bicalutamide.

Taking other medicines
Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription and herbal medicines. This is because Bicalutamide can affect the way other medicines work. Also some other medicines can affect the way Bicalutamide works.

If you take Bicalutamide 50mg together with one of the following medicines, the effect of bicalutamide as well as the other medicine may be influenced. Please speak to your doctor before taking any of these medicines together with Bicalutamide 50mg.

Bicalutamide might interfere with some medicines used to treat heart rhythm problems (e.g. quinidine, procainamide, amiodarone and sotalol) or might increase the risk of heart rhythm problems when used with some other drugs (e.g. methadone (used for pain relief and part of drug addiction detoxification), moxifloxacin (an antibiotic), antipsychotics used for serious mental illnesses).
- warfarin or any similar medicine to prevent blood clots,
- terfenadine or astemizole (for hay fever or allergy),
- cisapride (for stomach disorders),
- ciclosporin (used to suppress your immune system to prevent and treat rejection of a transplanted organ or bone marrow),
- calcium channel blockers (used to treat high blood pressure or some heart conditions)
- cimetidine (used to treat stomach ulcers),
- ketoconazole (used to treat fungal infections of the skin and nails)."

Taking Bicalutamide 50mg with food and drink
Bicalutamide 50mg can be taken before, during or after a meal, but also you can take them without food. The film coated tablet should be swallowed with some water or another liquid.

Pregnancy, breastfeeding and fertility
Bicalutamide 50mg is contra-indicated in females and must not be given to pregnant or breast-feeding mothers.

Driving and using machines
Bicalutamide 50mg is unlikely to adversely affect your ability to drive a car or to operate machinery. However, some people may occasionally feel dizzy or drowsy after taking Bicalutamide 50mg. If this happens to you, you should exercise caution when carrying out such tasks. If you suffer from dizziness or drowsiness you would be best advised not to carry out such tasks. However if you still drive a car or use machines you should exercise extra caution.

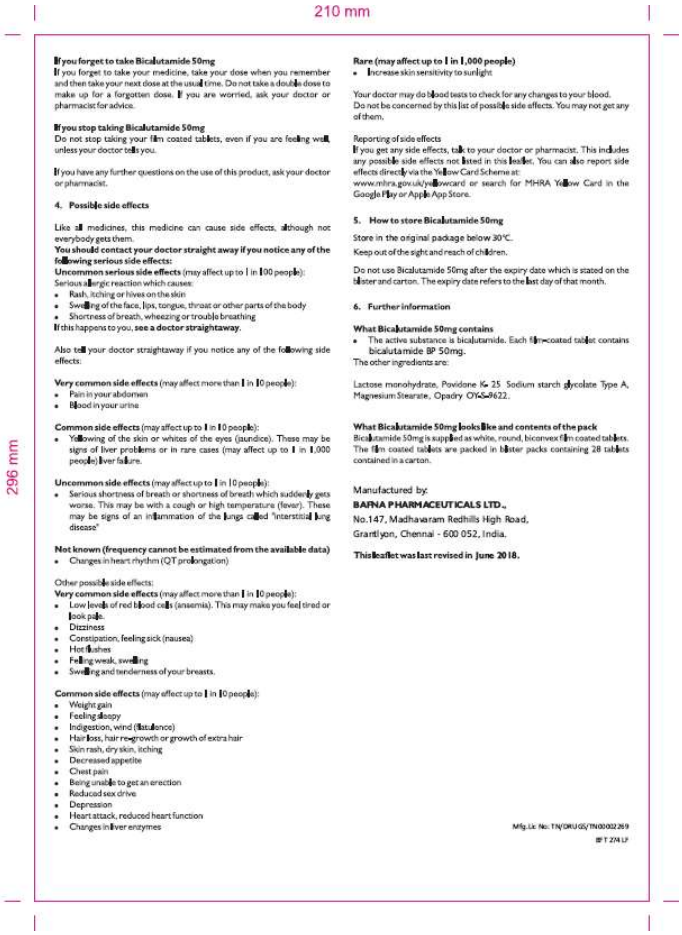
Important information about some of the ingredients of Bicalutamide 50mg
Bicalutamide 50mg contains lactose. If you have been told by your doctor that you have an intolerance to some sugars, such as lactose, contact your doctor immediately.

3. How to take Bicalutamide 50mg

Always take Bicalutamide 50mg exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure. The usual dose is one film coated tablet daily. It is better to take the film coated tablet at the same time every day. The film coated tablet should be swallowed with some water or another liquid without being chewed and can be taken with or without food.

Children and adolescents
This medicine is not recommended for patients under the age of 18 years.

If you take more Bicalutamide 50mg than you should
If you take more than your normal dose, contact your doctor. In the case of an overdose, contact the nearest hospital immediately. If possible, take your film-coated tablets or the box with you to show the doctor what you have taken.



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If you forget to take Bicalutamide 50mg
If you forget to take your medicine, take your dose when you remember and then take your next dose at the usual time. Do not take a double dose to make up for a forgotten dose. If you are worried, ask your doctor or pharmacist for advice.

If you stop taking Bicalutamide 50mg
Do not stop taking your film coated tablets, even if you are feeling well, unless your doctor tells you.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.
You should contact your doctor straight away if you notice any of the following serious side effects:
Uncommon serious side effects (may affect up to 1 in 100 people):
Serious allergic reaction which causes:
- Rash, itching or hives on the skin
- Swelling of the face, lips, tongue, throat or other parts of the body
- Shortness of breath, wheezing or trouble breathing

If this happens to you, see a doctor straightaway.

Also tell your doctor straightaway if you notice any of the following side effects:

Very common side effects (may affect more than 1 in 10 people):
- Pain in your abdomen
- Blood in your urine

Common side effects (may affect up to 1 in 10 people):
- Yellowing of the skin or whites of the eyes (jaundice). These may be signs of liver problems or in rare cases (may affect up to 1 in 1,000 people) liver failure.

Uncommon side effects (may affect up to 1 in 10 people):
- Serious shortness of breath or shortness of breath which suddenly gets worse. This may be with a cough or high temperature (fever). These may be signs of an inflammation of the lungs called "interstitial lung disease"

Not known (frequency cannot be estimated from the available data)
- Changes in heart rhythm (QT prolongation)

Other possible side effects:
Very common side effects (may affect more than 1 in 10 people):
- Low levels of red blood cells (anaemia). This may make you feel tired or look pale.
- Dizziness
- Constipation, feeling sick (nausea)
- Hot flushes
- Feeling weak, swelling
- Swelling and tenderness of your breasts.

Common side effects (may affect up to 1 in 10 people):
- Weight gain
- Feeling sleepy
- Indigestion, wind (flatulence)
- Hair loss, hair re-growth or growth of extra hair
- Skin rash, dry skin, itching
- Decreased appetite
- Chest pain
- Being unable to get an erection
- Reduced sex drive
- Depression
- Heart attack, reduced heart function
- Changes in liver enzymes

Rare (may affect up to 1 in 1,000 people)
- Increase skin sensitivity to sunlight

Your doctor may do blood tests to check for any changes to your blood. Do not be concerned by this list of possible side effects. You may not get any of them.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

5. How to store Bicalutamide 50mg

Store in the original package below 30°C.

Keep out of the sight and reach of children.

Do not use Bicalutamide 50mg after the expiry date which is stated on the blister and carton. The expiry date refers to the last day of that month.

6. Further information

What Bicalutamide 50mg contains
- The active substance is bicalutamide. Each film-coated tablet contains bicalutamide BP 50mg.

The other ingredients are:

Lactose monohydrate, Povidone K- 25 Sodium starch glycolate Type A, Magnesium Stearate, Opadry OY-S-9622.

What Bicalutamide 50mg looks like and contents of the pack
Bicalutamide 50mg is supplied as white, round, biconvex film coated tablets. The film coated tablets are packed in blister packs containing 28 tablets contained in a carton.

Manufactured by:
BAFNA PHARMACEUTICALS LTD.,
No.147, Madhavaram Redhills High Road,
Grantlyon, Chennai - 600 052, India.

This leaflet was last revised in June 2018.

Mfg.Lic No: TN/DRUGS/TN0002269
BPT 274 LP