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LAY SUMMARY

The MHRA granted Neolab Limited a Marketing Authorisation (licence) for the medicinal product Bicalutamide 50 mg Tablets on 14th July 2011.

Bicalutamide Tablets are used to treat prostate cancer.

This product contains the drug substance bicalutamide.

Bicalutamide is one of a group of medicines called anti-androgens. It has been shown that the growth of tumours of the prostate gland may be dependent on male hormones. Since bicalutamide blocks the action of androgens, it can be used to treat tumours of the prostate gland.

No new or unexpected safety concerns arose from this application and it was therefore judged that the benefits of taking Bicalutamide 50 mg Tablets outweigh the risks and a Marketing Authorisation was granted.
BICALUTAMIDE 50 MG TABLETS
PL 08137/0190

SCIENTIFIC DISCUSSION

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INTRODUCTION

The UK granted Neolab Limited a Marketing Authorisation for the medicinal product Bicalutamide 50 mg Tablets (PL 08137/0190) on 14th July 2011. This product is a prescription-only medicine for the treatment of advanced prostate cancer in combination with luteinizing hormone releasing hormone (LHRH) analogue therapy or surgical castration.

The application was submitted as an abridged application, according to Article 10.1 of Directive 2001/83/EC (as amended), claiming to be a generic medicinal product of Casodex 50 mg Film-coated Tablets, originally licensed to Zeneca Limited on 23rd February 1995 (PL 12619/0102). This reference licence then underwent a change of ownership on 18th June 2000 to AstraZeneca UK Limited (PL 17901/0005).

Bicalutamide is a non-steroidal anti-androgen, which is 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.

No new non-clinical studies were conducted, which is acceptable given that the product contains a widely-used, well-known active substance. No clinical studies with the exception of the bioequivalence study have been performed and none are required for this application because the pharmacology of bicalutamide is well-established.

It is considered that the pharmacovigilance system as described by the applicant fulfils the requirements and provides adequate evidence that the applicant has the services of a qualified person responsible for pharmacovigilance and has the necessary means for the notification of any adverse reaction suspected of occurring.

Satisfactory justification was provided for the absence of a Risk Management Plan.

No new or unexpected safety concerns arose from this application and it was therefore judged that the benefits of taking Bicalutamide 50 mg Tablets outweigh the risks and a Marketing Authorisation was granted.
PHARMACEUTICAL ASSESSMENT

DRUG SUBSTANCE
Bicalutamide

INN: Bicalutamide

Chemical name: \((\pm)-N-[4\text{-Cyano-3-(trifluoromethyl)phenyl}]\)-3-\([4\text{-fluorophenyl}]\) sulfonyl]-2-hydroxy-2-methylpropanamide

Structural formula:

\[
\text{R-enantiomer} \quad \text{and} \quad \text{S-enantiomer}
\]

Molecular formula: \(C_{18}H_{14}F_{4}N_{2}O_{4}S\)

Molecular weight: 430.38

Appearance: White crystalline powder

Solubility: Freely soluble in N,N-dimethylformamide and acetone, sparingly soluble in methanol and acetonitrile and practically insoluble in water and buffer solutions.

Bicalutamide complies with in-house specifications.

Synthesis of the drug substance from the designated starting materials has been adequately described and appropriate in-process controls and intermediate specifications are applied.

Satisfactory specifications are in place for all starting materials and reagents, and these are supported by relevant Certificates of Analysis.

Appropriate proof of structure data have been supplied for the drug substance. All potential known impurities have been identified and characterised.

An appropriate specification is provided for the drug substance, with suitable test methods and limits. Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications. Batch analysis data are provided, which comply with the proposed specification. Satisfactory Certificates of Analysis have been provided for all reference standards used.

Satisfactory specifications and Certificates of Analysis have been provided for all aspects of the container-closure system. A declaration has been provided that the primary packaging complies with current regulations concerning contact with foodstuff.
Appropriate stability data have been generated, which show the drug substance to be a physically and chemically stable drug, and which support an appropriate retest period.

**DRUG PRODUCT**

**Other ingredients**

Other ingredients in the tablet core consist of the pharmaceutical excipients lactose monohydrate, maize starch, povidone, crospovidone, colloidal anhydrous silica, sodium lauryl sulphate and magnesium stearate

The film coating consists of titanium dioxide (E171), hypromellose and macrogol.

All of the ingredients comply with the relevant monographs in the European Pharmacopoeia.

With the exception of lactose monohydrate and magnesium stearate, none of the excipients contain material of animal or human origin. The applicant has provided a declaration that the milk used in the production of the lactose monohydrate is sourced from healthy animals under the same conditions as those intended for human consumption.

The supplier of magnesium stearate has confirmed that the material is of animal origin and a valid Transmissible Spongiform Encephalopathies (TSE) Certificate of Suitability has been provided.

**Product development**

The objective of the development programme was to produce a product containing bicalutamide that could be considered a generic medicinal product of Casodex 50 mg Film-coated Tablets.

The applicant has provided suitable evidence of product development. Justification for the use and amount of each excipient has been provided and is valid. Comparative impurity and dissolution profiles have been provided for the finished product versus the reference product Casodex 50 mg Film-coated Tablets.

**Manufacture**

A description and flow-chart of the manufacturing method has been provided.

In-process controls are satisfactory and are based on process validation data and controls on the finished product. Process validation data on production-scale batches have been provided and are satisfactory.

**Finished product specification**

The finished product specification is satisfactory. Test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and comply with the release specification. Certificates of Analysis for all working standards have been provided and are satisfactory.

**Container-Closure System**

The product is packaged in polyvinylchloride (PVC) and aluminium foil blister packs in outer cardboard cartons containing 28 film-coated tablets.

Satisfactory specifications and Certificates of Analysis have been provided for all packaging components. All primary product packaging complies with EU legislation regarding contact with food.
Stability
Finished product stability studies have been conducted in accordance with current guidelines. Based on the results, a shelf-life of 3 years has been set, with no special storage conditions. This is satisfactory.

ADMINISTRATIVE
Expert Report
A pharmaceutical expert report has been written by a suitably qualified person and is satisfactory.

Summary of Product Characteristics (SmPC)
This is satisfactory.

Labelling
This is satisfactory.

Patient Information Leaflet (PIL)
This is satisfactory.

A package leaflet has been submitted to the MHRA along with results of consultations with target patient groups ("user testing"), in accordance with Article 59 of Council Directive 2001/83/EC, as amended. The results indicate that the package leaflet is well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that it contains.

MAA Form
This is satisfactory.

Conclusion
From a pharmaceutical point of view, it is recommended that a Marketing Authorisation is granted for this application.
NON-CLINICAL ASSESSMENT

The pharmacodynamics, pharmacokinetics and toxicological properties of bicalutamide are well-known. As bicalutamide is a widely used, well-known active substance, the applicant has not provided any additional studies and none are required.

The non-clinical expert report has been written by an appropriately qualified person and is a suitable summary of the non-clinical aspects of the dossier.

An Environmental Risk Assessment was not submitted or required for this generic application.
CLINICAL ASSESSMENT

CLINICAL PHARMACOLOGY
To support the application, the Marketing Authorisation Holder has included a single bioequivalence study:

Pharmacokinetics

A single dose, randomised, two-treatment parallel bioequivalence study comparing the pharmacokinetics of Bicalutamide 50 mg Tablets (Test) versus Casodex (bicalutamide) 50 mg Tablets (Reference) in fasted volunteers.

All subjects were in a fasted state before dosing. Blood sampling was performed pre- and up to 671 hours post dose in each treatment period. Pharmacokinetic parameters were measured from the plasma and analysed statistically.

Pharmacokinetic data from this study are presented below as log-transformed values:

<table>
<thead>
<tr>
<th>Treatment</th>
<th>(AUC_{0-t}) (ng.h/ml)</th>
<th>(AUC_{0-\infty}) (ng.h/ml)</th>
<th>(C_{\text{max}}) (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test, T (geometric mean)</td>
<td>177,258.47</td>
<td>188,084.01</td>
<td>943.94</td>
</tr>
<tr>
<td>Reference, R (geometric mean)</td>
<td>177,988.22</td>
<td>188,698.43</td>
<td>969.51</td>
</tr>
<tr>
<td>Ratio T/R (90% CI)</td>
<td>99.59</td>
<td>99.67</td>
<td>97.36</td>
</tr>
<tr>
<td>90% Confidence Interval</td>
<td>(87.68 – 113.12)</td>
<td>(87.88 – 113.06)</td>
<td>(87.05 – 108.89)</td>
</tr>
</tbody>
</table>

AUC\(_{0-\infty}\) area under the plasma concentration-time curve from time zero to infinity
AUC\(_{0-t}\) area under the plasma concentration-time curve from time zero to \(t\) hours
\(C_{\text{max}}\) maximum plasma concentration

The results for the primary variables indicated that the 90% confidence intervals for the test/reference ratio of geometric means for \(AUC_{0-t}\) and \(C_{\text{max}}\) for bicalutamide lie within 80.00-125.00% boundaries. Bioequivalence has been shown between the test and reference products in this study.

EFFICACY
No new data has been provided and none are required for this generic application.

SAFETY
No new data has been provided and none are required for this generic application.

EXPERT REPORTS
The clinical expert report has been written by a suitably qualified person and is satisfactory.

PATIENT INFORMATION LEAFLET (PIL)
This is consistent with that for the reference product and is satisfactory.

LABELLING
This is satisfactory.
APPLICATION FORM (MAA)
This is satisfactory.

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)
This is consistent with that for the reference product and is satisfactory.

DISCUSSION
The applicant has demonstrated bioequivalence between the test and reference product satisfactorily.

CLINICAL CONCLUSION
The bioequivalence study submitted has shown that the applicant’s Bicalutamide 50 mg Tablets can be considered a generic medicinal product of the reference product Casodex 50 mg Tablets.

From a clinical point of view, it is recommended that a Marketing Authorisation is granted for this application.
OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY
The important quality characteristics of Bicalutamide 50 mg Tablets are well-defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

NON-CLINICAL
No new non-clinical data were submitted and none are required for an application of this type.

EFFICACY
Bioequivalence has been demonstrated between the applicant’s Bicalutamide 50 mg Tablets and the reference product Casodex 50 mg Tablets.

No new or unexpected safety concerns arise from this application.

The SmPC, PIL and labelling are satisfactory and consistent with those for the reference product.

RISK BENEFIT ASSESSMENT
The quality of the products is acceptable and no new non-clinical or clinical safety concerns have been identified. The bioequivalence study supports the claim that the applicant’s product and the reference product are interchangeable. Extensive clinical experience with bicalutamide is considered to have demonstrated the therapeutic value of the compound. The benefit/risk ratio is considered to be positive.
**BICALUTAMIDE 50 MG TABLETS**  
**PL 08137/0190**

**STEPS TAKEN FOR ASSESMENT**

<p>| | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>1</td>
<td>The MHRA received the Marketing Authorisation application on 31st March 2008.</td>
</tr>
<tr>
<td>2</td>
<td>Following standard checks and communication with the applicant the MHRA considered the application valid on 8th April 2008.</td>
</tr>
<tr>
<td>3</td>
<td>Following assessment of the application, the MHRA requested further information relating to the dossier on 28th June 2008, 21st July 2010 and 26th April 2011.</td>
</tr>
<tr>
<td>4</td>
<td>The applicant responded to the MHRA’s requests, providing further information on 25th February 2010, 22nd October 2010 and 21st June 2011.</td>
</tr>
<tr>
<td>5</td>
<td>The application was determined on 14th July 2011.</td>
</tr>
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</table>
BICALUTAMIDE 50 MG TABLETS
PL 08137/0190

STEPS TAKEN AFTER ASSESSMENT

<table>
<thead>
<tr>
<th>Date submitted</th>
<th>Application type</th>
<th>Scope</th>
<th>Outcome</th>
</tr>
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<tbody>
<tr>
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</tbody>
</table>
SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Bicalutamide 50 mg Tablets.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each tablet contains 50 mg bicalutamide.
Each tablet contains 61 mg lactose monohydrate.
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Film-coated tablet.
White round, biconvex film-coated tablet embossed ‘B50’ on one side and plain on other side.

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
Treatment of advanced prostate cancer in combination with LHRH analogue therapy or surgical castration.

4.2 Posology and method of administration
Adult males including the elderly: one tablet (50mg) 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.

Children: Bicalutamide is contra-indicated 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 (see Section 4.4).

4.3 Contraindications
Bicalutamide is contra-indicated in females and children.
Bicalutamide must not be given to any patient who has shown a hypersensitivity reaction to its use.
Co-administration of terfenadine, astemizole or cisapride with bicalutamide is contra-indicated.

4.4 Special warnings and precautions for use
Bicalutamide 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 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 have been observed rarely with bicalutamide (see Section 4.8). 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 agonist.

Bicalutamide has been shown to inhibit Cytochrome P450 (CYP 3A4), as such caution should be exercised when co-administered with drugs metabolised predominantly by CYP 3A4, see Sections 4.3 and 4.5.

Bicalutamide Tablets contain lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take these tablets.
4.5 Interaction with other medicinal products and other forms of interaction

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 contra-indicated 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 cyclosporin, 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.

4.6 Pregnancy and lactation

Bicalutamide is contra-indicated in females and must not be given to pregnant women or nursing mothers.

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 (≥ 1/1000 to ≤ 1/100); rare (≥ 1/10,000 to ≤ 1/1000); very rare (≤ 1/10,000); not known (can not be estimated from the available data).

<table>
<thead>
<tr>
<th>System Organ Class</th>
<th>Frequency</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood and lymphatic system disorders</td>
<td>Very common</td>
<td>Anaemia</td>
</tr>
<tr>
<td>Immune system disorders</td>
<td>Uncommon</td>
<td>Hypersensitivity, angioedema and urticaria</td>
</tr>
<tr>
<td>Metabolism and nutrition disorders</td>
<td>Common</td>
<td>Decreased appetite</td>
</tr>
<tr>
<td>Psychiatric disorders</td>
<td>Common</td>
<td>Decreased libido depression</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>Very common</td>
<td>Dizziness</td>
</tr>
<tr>
<td>Cardiac disorders</td>
<td>Common</td>
<td>Somnolence</td>
</tr>
<tr>
<td>Vascular disorders</td>
<td>Very common</td>
<td>Hot flush</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td>Uncommon</td>
<td>Interstitial lung disease. Fatal outcomes have been reported.</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>Very common</td>
<td>Abdominal pain Constipation nausea</td>
</tr>
</tbody>
</table>

Common | Dyspepsia
<table>
<thead>
<tr>
<th>Medical Conditions</th>
<th>Frequency</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepato-biliary disorders</td>
<td>Common</td>
<td>Flatulence, Hepatotoxicity, jaundice, raised transaminases</td>
</tr>
<tr>
<td></td>
<td>Rare</td>
<td>Hepatic failure. Fatal outcomes have been reported.</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>Common</td>
<td>Alopecia, Hirsuitism/hair re-growth, Dry skin, Pruritis, Rash</td>
</tr>
<tr>
<td>Renal and urinary disorders</td>
<td>Very common</td>
<td>Haematuria</td>
</tr>
<tr>
<td>Reproductive system and breast disorders</td>
<td>Very common</td>
<td>Gynaecomastia and breast tenderness</td>
</tr>
<tr>
<td></td>
<td>Common</td>
<td>Erectile dysfunction</td>
</tr>
<tr>
<td>General disorders and administrative site conditions</td>
<td>Very common</td>
<td>Asthenia, Oedema</td>
</tr>
<tr>
<td>Investigations</td>
<td>Common</td>
<td>Chest pain</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Weight gain</td>
</tr>
</tbody>
</table>

1. Hepatic changes are rarely severe and were frequently transient, resolving or improving with continued therapy or following cessation of therapy.
2. Hepatic failure has occurred rarely in patients treated with Bicalutamide, but a casual relationship has not been established with certainty. Periodic liver function testing should be considered (see also section 4.4).
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 appears to be increased when bicalutamide 50 mg was used in combination with LHRH agonists but no increase in risk was evident when bicalutamide 150 mg was used as a monotherapy to treat prostate cancer.

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
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. Clinically, discontinuation of Bicalutamide can result in antiandrogen withdrawal syndrome in a subset of patients.
Bicalutamide is a racemate with its antiandrogenic activity being almost exclusively in the (R)-enantiomer.

5.2 Pharmacokinetic properties
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 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.
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 (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 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.

5.3 Preclinical safety data
Bicalutamide is a potent antiandrogen 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.

6 PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Tablet core:
- Lactose monohydrate
- Maize starch
- Povidone
- Crospovidone
- Colloidal anhydrous silica
- Sodium lauryl sulphate
- Magnesium stearate

Film coating material:
- Titanium dioxide (E171)
- Hypromellose
- Macrogol 400

6.2 Incompatibilities
None known

6.3 Shelf life
3 years.

6.4 Special precautions for storage
There are no special conditions for storage.

6.5 Nature and contents of container
PVC/aluminium foil blister packs in an outer cardboard carton containing 28 film-coated tablets.

6.6 Special precautions for disposal
No special requirements.

7 MARKETING AUTHORISATION HOLDER
Neolab Limited
57 High Street
Odiham
Hants
RG29 1LF

8 MARKETING AUTHORISATION NUMBER(S)
PL 08137/0190
9  DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
14/07/2011

10 DATE OF REVISION OF THE TEXT
14/07/2011
PATIENT INFORMATION LEAFLET

Bicalutamide 50 mg Tablets
(bicalutamide)

The name of this medicine is Bicalutamide 50 mg Tablets, which will be referred to as Bicalutamide Tablets throughout this leaflet.

Read all of this leaflet carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or pharmacist.
- This medicine has been prescribed for you personally and you should 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 Tablets are and what they are used for.
2. Before you take Bicalutamide Tablets.
3. How to take Bicalutamide Tablets.
4. Possible side effects.
5. How to store Bicalutamide Tablets.
6. Further information.

1. WHAT BICALUTAMIDE TABLETS ARE AND WHAT THEY ARE USED FOR

Bicalutamide Tablets are used to treat prostate cancer.

Bicalutamide is one of a group of medicines called anti-androgens. It has been shown that the growth of tumours of the prostate gland may be dependent on male hormones. Since bicalutamide blocks the action of androgens, it can be used to treat tumours of the prostate gland.

2. BEFORE YOU TAKE BICALUTAMIDE TABLETS

Do not take Bicalutamide Tablets if you are:
- allergic to bicalutamide or to any of the other ingredients in the tablets (these are listed in section 6, Further Information)
- a woman or a child
- if you are taking the medicines terfenadine or astemizole (antihistamines) or cisapride (for some types of indigestion).

Take special care with Bicalutamide Tablets
Before you take Bicalutamide Tablets you should tell your doctor if you:
- have liver problems
- have diabetes and are already taking an ‘LHRH analogue’. These include goserelin, buserelin, leuprorelin and triptorelin.
- have been told you have an intolerance to some sugars. Each Bicalutamide Tablet contains 61 mg of lactose monohydrate.

If any of the above apply to you talk to your doctor who will decide what to do.
Taking other medicines
You should tell your doctor if you are taking or have taken any of the following medicines as they may interact with your Bicalutamide Tablets:

- oral anticoagulants (such as warfarin) used to thin the blood
- calcium channel blockers (such as verapamil or diltiazem) used to treat high blood pressure or some heart conditions
- cimetidine (used to treat ulcers)
- ketoconazole (used to treat fungal infections)
- ciclosporin (used to suppress the immune system following transplant surgery).

It may still be all right for you to take Bicalutamide Tablets and your doctor will be able to decide what is suitable for you.

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Pregnancy and breast-feeding
Women must not take Bicalutamide Tablets.

Driving and using machines
Some people may occasionally feel drowsy when taking Bicalutamide Tablets. If this happens to you, you should exercise caution if you drive or operate machinery.

Important information about some of the ingredients of Bicalutamide Tablets
These tablets contain lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

3. HOW TO TAKE BICALUTAMIDE TABLETS

Dosage
Always take Bicalutamide Tablets exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

The usual dose for Bicalutamide Tablets is as follows:-
Adults and elderly men: the dose is one tablet daily. The tablet should be swallowed whole with plenty of water. Take your tablet at the same time each day.

Bicalutamide Tablets are not suitable for use by females.

If you take more Bicalutamide Tablets than you should
If you have accidentally taken more than your prescribed dose, contact your doctor or pharmacist immediately. Remember to take the pack and any remaining tablets with you.

If you forget to take your dose of Bicalutamide Tablets
Do not worry. Take your dose when you remember and then take your next dose at the usual time. Do not take two doses at the same time.

If you have any further questions on the use of this product, ask your doctor or pharmacist for advice.
4. POSSIBLE SIDE EFFECTS

Like all medicines, Bicalutamide can cause side effects, although not everybody gets them.

Allergic reactions:
These are uncommon (affect less than 1 in 100 people). The symptoms can include sudden onset of:
- 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 straight away.

Also tell your doctor straight away if you notice any of the following:

Very common (affects more than 1 in 10 people):
- Pain in your abdomen
- Blood in your urine

Common (affects less than 1 in 10 people):
- Yellowing of the skin or whites of your eyes (jaundice). These may be signs of liver problems or in rare cases (affects less than 1 in 1,000 people) liver failure

Uncommon (affects less than 1 in 100 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’
- Hypersensitivity, angioedema (serious allergic reaction which causes swelling of the face or throat), urticaria (hives)
- Cardiac failure

Other possible side effects:

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

Common (affects less than 1 in 10 people)
- Decreased appetite
- Reduced sex drive
- Depression
- Feeling sleepy
- Indigestion
- Wind (flatulence)
- Hair loss
- Hair re-growth or growth of extra hair
- Dry skin
- Itching
- Skin rash
• Being unable to get an erection (impotence)
• Weight gain
• Chest pain
• Hepatotoxicity, jaundice, raised transaminases.

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.
If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE BICALUTAMIDE TABLETS

Keep Bicalutamide Tablets out of the sight and reach of children.

Store in the original package to protect the tablets from moisture.

Do not use Bicalutamide Tablets after the expiry date which is stated on the carton after EXP. The expiry date refers to the last day of that month.

Medicines should not be disposed of via wastewater or household waste. If you have any Bicalutamide Tablets left after completing your course of treatment, please return them to your pharmacist who will dispose of them safely. These measures will help protect the environment.

6. FURTHER INFORMATION

What Bicalutamide Tablets contain:
The active substance is bicalutamide. Each tablet contains 50 mg of bicalutamide.

The other ingredients are lactose monohydrate, maize starch, sodium lauryl sulphate, povidone, crospovidone, colloidal anhydrous silica, magnesium stearate, hypromellose, macrogol and titanium dioxide (E171).

What Bicalutamide Tablets look like and the contents of the pack:
Bicalutamide 50 mg Tablets are white, round, film-coated tablets.
Your medicine is available in blisters containing 28 tablets.

Marketing Authorisation Holder and Manufacturer:
Neolab Limited Ltd, 57 High Street, Odiham, Hants, RG29 1LF.

This information is available in alternative formats upon request.

This leaflet was last approved in June 2011.
LABELLING

Carton:

Bicalutamide 50 mg Tablets

Each tablet contains 50 mg bicalutamide. Also contains lactose (see enclosed leaflet). For oral administration only.

Dosage: To be taken as directed by your doctor.

Please read the enclosed leaflet carefully before use.

Store in the original package.

Keep out of the reach and sight of children.

28 Film-coated Tablets

Bicalutamide 50 mg Tablets

28 Film-coated Tablets

Bicalutamide 50 mg Tablets

PL 08137/0190

MA Holder: Neolab Limited, 57 High Street, Odiham, Hants, RG29 1LF
Bicalutamide 50 mg Tablets

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**Blister:**

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