APPROVED PACKAGE INSERT

UPDATE ACCORDING TO DEC 2013 PI GUIDELINE ***DATE SUBMITTED TO MCC: 5/02/2015***

MODULE 1.3.1.1 – Package Insert

Product proprietary name:	***Accord Bicalutamide 50 mg***
Dosage form and strength:	***50 mg Bicalutamide per Film Coated Tablet***
Applicant/PHCR:	***Accord Healthcare (Pty) Ltd***

SCHEDULING STATUS:

S4

PROPRIETARY NAME AND DOSAGE FORM:

Accord Bicalutamide 50 mg (Film coated tablets)

COMPOSITION:

Each tablet contains 50 mg bicalutamide.

Contains lactose monohydrate.

PHARMACOLOGICAL CLASSIFICATION:

A 21.12 Hormone inhibitors

PHARMACOLOGICAL ACTION:

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. Bicalutamide is a racemate with its anti-androgenic activity being almost exclusively in the (R) - enantiomer. Bicalutamide is an anti-androgen 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.

Pharmacokinetic properties:

Bicalutamide is highly plasma protein bound and extensively metabolised (via oxidation and glucuronidation); its metabolites are eliminated via the kidneys and bile in approximately equal portions.

INDICATIONS:

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

Amendments have been effected according to MCC recommendations, and the package insert is free of typographical and grammatical errors.

Initials:

UPDATE ACCORDING TO DEC 2013 PI GUIDELINE ***DATE SUBMITTED TO MCC: 5/02/2015***

MODULE 1.3.1.1 – Package Insert

Product proprietary name:	***Accord Bicalutamide 50 mg***
Dosage form and strength:	***50 mg Bicalutamide per Film Coated Tablet***
Applicant/PHCR:	***Accord Healthcare (Pty) Ltd***

CONTRA-INDICATIONS:

Females and children, pregnant women or breastfeeding mothers.

Accord Bicalutamide 50 mg must not be given to any patient who has shown a hypersensitivity reaction to its use.

WARNINGS AND SPECIAL PRECAUTIONS:

Hepatic function impairment:

Accord Bicalutamide 50 mg 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 Accord Bicalutamide 50 mg.

Metabolism of Accord Bicalutamide 50 mg may be delayed in patients with moderate to severe hepatic function impairment, resulting in a prolonged elimination half-life and increased risk of toxicity. Therefore, Accord Bicalutamide 50 mg should be used with caution in patients with moderate to severe hepatic impairment.

Periodic liver function testing should be considered during long-term use of Accord Bicalutamide 50 mg, due to the possibility of hepatic changes. Severe hepatic changes have been observed infrequently with Accord Bicalutamide 50 mg (see "Side effects"). Accord Bicalutamide 50 mg therapy should be discontinued if changes are severe.

Medicines metabolised by cytochrome P450:

Although clinical studies using antipyrine as a marker of Cytochrome P450 (CYP) activity showed no evidence of a drug interaction potential with Accord Bicalutamide 50 mg, midazolam exposure (AUC) was increased by up to 80 %, after co-administration with Accord Bicalutamide 50 mg for 28 days. This rise is comparable to that seen in other studies after administration of grapefruit juice.

Caution should be exercised with the co-administration of Accord Bicalutamide 50 mg with compounds

Amendments have been effected according to MCC recommendations, and the package insert is free of typographical and grammatical errors.

Initials: 

UPDATE ACCORDING TO DEC 2013 PI GUIDELINE ***DATE SUBMITTED TO MCC: 5/02/2015***

MODULE 1.3.1.1 – Package Insert

Product proprietary name:	***Accord Bicalutamide 50 mg***
Dosage form and strength:	***50 mg Bicalutamide per Film Coated Tablet***
Applicant/PHCR:	***Accord Healthcare (Pty) Ltd***

such as these.

Effects on ability to drive and use machines:

Accord Bicalutamide 50 mg is unlikely to impair the ability of patients to drive or operate machinery.

INTERACTIONS:

Luteinising Hormone Releasing Hormone (LHRH):

There is no evidence of any pharmacodynamic or pharmacokinetic interactions between Accord Bicalutamide 50 mg and LHRH analogues.

Ketoconazole and Cimetidine:

Formal interaction studies have not been undertaken, but caution should be exercised when prescribing Accord Bicalutamide 50 mg with other medicines, e.g. ketoconazole and cimetidine, which may inhibit oxidation of Accord Bicalutamide 50 mg. It could result in increased plasma concentrations of Accord Bicalutamide 50 mg which could lead to an increase in side-effects.

Medicines Metabolised by Cytochrome P450:

Although clinical studies using antipyrine as a marker of Cytochrome P450 (CYP) activity showed no evidence of a drug interaction potential with Accord Bicalutamide 50 mg, midazolam exposure (AUC) was increased by up to 80 %, after co-administration with Accord Bicalutamide 50 mg for 28 days. This rise is comparable to that seen in other studies after administration of grapefruit juice. Caution should be exercised with the co-administration of Accord Bicalutamide 50 mg with compounds such as these, (see "Warnings and Special Precautions").

Coumarin Anticoagulants:

Amendments have been effected according to MCC recommendations, and the package insert is free of typographical and grammatical errors.

Initials:

UPDATE ACCORDING TO DEC 2013 PI GUIDELINE ***DATE SUBMITTED TO MCC: 5/02/2015***

MODULE 1.3.1.1 – Package Insert

Product proprietary name:	***Accord Bicalutamide 50 mg***
Dosage form and strength:	***50 mg Bicalutamide per Film Coated Tablet***
Applicant/PHCR:	***Accord Healthcare (Pty) Ltd***

Accord Bicalutamide 50 mg can displace the coumarin anticoagulant, warfarin, from its protein binding sites. It is therefore recommended that if Accord Bicalutamide 50 mg is started in patients who are already receiving coumarin anticoagulants, prothrombin time should be closely monitored.

PREGNANCY AND LACTATION:

Safety and efficacy of Accord Bicalutamide 50 mg during pregnancy and lactation have not been established, (see "Contra-indications").

DOSAGE AND DIRECTIONS FOR USE:

Adult males including the elderly:

One tablet (50 mg) once a day. Treatment with Accord Bicalutamide 50 mg should be started at least three days before commencing treatment with a 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 (see under "Warnings and Special Precautions").

SIDE EFFECTS:

Blood and lymphatic system disorders

Frequent: Anaemia

The following side effects have been reported but the frequencies are unknown: Leucopenia, neutropenia, thrombocytopenia

Amendments have been effected according to MCC recommendations, and the package insert is free of typographical and grammatical errors.

Initials:

UPDATE ACCORDING TO DEC 2013 PI GUIDELINE ***DATE SUBMITTED TO MCC: 5/02/2015***

MODULE 1.3.1.1 – Package Insert

Product proprietary name:	***Accord Bicalutamide 50 mg***
Dosage form and strength:	***50 mg Bicalutamide per Film Coated Tablet***
Applicant/PHCR:	***Accord Healthcare (Pty) Ltd***

Immune system disorders

Less frequent: Hypersensitivity reactions (including angioneurotic oedema and urticaria)

Metabolism and nutrition disorders

Frequent: Anorexia

The following side effects have been reported but the frequencies are unknown: Diabetes mellitus, hyperglycaemia

Psychiatric disorders

Frequent: depression

Nervous system disorders

Frequent: Dizziness, somnolence, insomnia

Less frequent: Reversible neurological reactions such as nervousness, drowsiness and confusion

Vascular disorders

Frequent: Hypertension

Respiratory, thoracic and mediastinal disorders

Frequent: Upper respiratory tract infection, cough or hoarseness, shortness of breath, sore throat and sneezing

Less frequent: Interstitial lung disease and dyspnoea. Fatal outcomes have been reported.

Gastrointestinal disorders

Frequent: Abdominal pain, constipation, nausea, dyspepsia, flatulence, diarrhoea

Amendments have been effected according to MCC recommendations, and the package insert is free of typographical and grammatical errors.

Initials: W

UPDATE ACCORDING TO DEC 2013 PI GUIDELINE ***DATE SUBMITTED TO MCC: 5/02/2015***

MODULE 1.3.1.1 – Package Insert

Product proprietary name:	***Accord Bicalutamide 50 mg***
Dosage form and strength:	***50 mg Bicalutamide per Film Coated Tablet***
Applicant/PHCR:	***Accord Healthcare (Pty) Ltd***

Less frequent: Gastro-intestinal or rectal bleeding, vomiting

Hepato-biliary disorders

Frequent: Hepatic changes (including elevated levels of transaminases, jaundice), hepatitis

Less frequent: Hepatic failure.

The following side effects have been reported but the frequencies are unknown: Methaemoglobinaemia

Skin and subcutaneous tissue disorders

Frequent: Alopecia, hirsuitism/hair re-growth, dry skin, pruritis, rash, sweating

Renal and urinary disorders

Frequent: Haematuria

The following side effects have been reported but the frequencies are unknown: Nocturia

Reproductive system and breast disorders

Frequent: Gynaecomastia and breast tenderness, impotence, decreased libido

General disorders and administration site conditions

Frequent: Asthenia, oedema, chest pain, fever, chills, flu-like syndrome

Investigations

Frequent: Weight gain

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

There is no human experience of overdosage. There is no specific antidote; treatment should be

Amendments have been effected according to MCC recommendations, and the package insert is free of typographical and grammatical errors.

Initials:

UPDATE ACCORDING TO DEC 2013 PI GUIDELINE ***DATE SUBMITTED TO MCC: 5/02/2015***

MODULE 1.3.1.1 – Package Insert

Product proprietary name:	***Accord Bicalutamide 50 mg***
Dosage form and strength:	***50 mg Bicalutamide per Film Coated Tablet***
Applicant/PHCR:	***Accord Healthcare (Pty) Ltd***

symptomatic. Dialysis may not be helpful, since Accord Bicalutamide 50 mg is highly protein bound and is not recovered unchanged in the urine. General supportive care, including frequent monitoring of vital signs, is indicated.

IDENTIFICATION:

White to off-white, round, biconvex, film coated tablets debossed 'B 50' on one side and plain on other side.

PRESENTATION:

Accord Bicalutamide 50 mg Tablets: 10 tablets per Clear PVC / PVdC-Aluminium blister strip, supplied in a pack size of 30.

STORAGE INSTRUCTIONS:

Store at or below 25 °C. Store in original package.

Keep out of reach of children.

REGISTRATION NUMBER:

42/21.12/0431

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

Accord Healthcare (Pty) Ltd

Tuscany Office Park

6 Coombe Place, Rivonia

Gauteng, South Africa

DATE OF PUBLICATION OF THE PACKAGE INSERT:

26 November 2010

5 February 2015

Amendments have been effected according to MCC recommendations, and the package insert is free of typographical and grammatical errors.

Initials: