SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Casodex 50 mg Film-coated Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 50 mg bicalutamide (INN)

Excipient(s) with known effect:

Each tablet contains 61 mg lactose monohydrate. For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

White film-coated tablet.

4. CLINICAL PARTICULARS

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 Casodex 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 (see section 4.4). Paediatric population: Casodex is contraindicated for use in children (see section 4.3).

4.3 Contraindications

Casodex is contraindicated in females and children (see section 4.6). Hypersensitivity to the active substance or to any of the excipients listed in section 6.1. Co-administration of terfenadine, astemizole or cisapride with Casodex is contraindicated (see section 4.5).

4.4 Special warnings and precautions for use

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

Casodex therapy. Severe hepatic changes and hepatic failure have been observed rarely with Casodex, and fatal outcomes have been reported (see section 4.8). Casodex 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 Casodex in combination with LHRH agonists. Casodex has been shown to inhibit cytochrome P450 (CYP3A4), as such caution should be exercised when co-administered with drugs metabolised predominantly by CYP3A4 (see sections 4.3 and 4.5). 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 (see section 4.5) 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 (see sections 4.5 and 4.8).

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine. This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of

interaction There is no evidence of any pharmacodynamic or pharmacokinetic interactions between Casodex 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 Casodex, mean midazolam exposure (AUC) was increased by up to 80%, after co-administration of Casodex 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 (see section 4.3) and caution should be exercised with the co-administration of Casodex 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 Casodex therapy. Caution should be exercised when prescribing Casodex with other drugs which may inhibit drug oxidation e.g. cimetidine and ketoconazole. In theory, this could result in increased plasma concentrations of Casodex 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 Casodex. It is therefore recommended that if Casodex is administered in patients who are concomitantly receiving coumarin anticoagulants, PT/INR should be closely monitored and adjustments of anticoagulant dose considered (see sections 4.4 and 4.8). Since androgen deprivation treatment may prolong the QT interval, the concomitant use of Casodex 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 (see section 4.4). Paediatric population Interaction studies have only been performed in adults.

4.5 Interaction with other medicinal products and other forms of interaction

Not provided in the source SmPC.

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 (see section 5.3). A period of subfertility or infertility should be assumed in man.

4.7 Effects on ability to drive and use machines

Casodex 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 Very common Anaemia system disorders Immune system disorders Uncommon Hypersensitivity, angioedema and urticaria Metabolism and nutrition Common Decreased appetite disorders Psychiatric disorders Common Decreased libido depression Nervous system Very common Dizziness disorders Common Somnolence Cardiac disorders Common Myocardial infarction (fatal outcomes have been reported)4, cardiac failure4 Not known QT prolongation (see sections 4.4 and 4.5). Vascular disorders Very common Hot flush Respiratory, thoracic and Uncommon Interstitial lung disease5 mediastinal disorders (fatal 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 Common Alopecia tissue disorders hirsutism/hair re-growth dry skin pruritus rash Rare Photosensitivity reaction Renal and urinary Very common Haematuria disorders Reproductive system and Very common Gynaecomastia and breast disorders breast tenderness3 Common Erectile dysfunction General disorders and Very common Asthenia administration site oedema conditions 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 (see sections 4.4. and 4.5). 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. Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

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

5.2 Pharmacokinetic properties

Absorption Casodex is well absorbed following oral administration. There is no evidence of any clinically relevant effect of food on bioavailability. Distribution Casodex 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 Casodex, 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

Casodex. 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 Casodex 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 eliminated from plasma.

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. Atrophy of seminiferous tubules of the testes is a predicted class effect with antiandrogens and has been observed for all species examined. Reversal of testicular atrophy occurred 4 months after the completion of dosing in a 6-month rat study (at doses of approximately 1.5 times human therapeutic concentrations at the recommended dose of 50 mg). No recovery was observed at 24 weeks after the completion of dosing in a 12-month rat study (at doses of approximately 2 times human concentrations at the recommended human dose of 50 mg). Following 12-months of repeated dosing in dogs (at doses of approximately 7 times human therapeutic concentrations at the recommended human dose of 50 mg), the incidence of testicular atrophy was the same in dosed and control dogs after a 6 month recovery period. In a fertility study (at doses of approximately 1.5 times human therapeutic concentrations at the recommended human dose of 50 mg), male rats had an increased time to successful mating immediately after 11 weeks of dosing; reversal was observed after 7 weeks offdose.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Casodex includes the following excipients:

Lactose Monohydrate Magnesium Stearate Hypromellose Macrogol 300 Povidone Sodium Starch Glycolate Titanium Dioxide (E171).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

5 years.

6.4 Special precautions for storage

Do not store above 30°C.

6.5 Nature and contents of container

PVC blister/aluminium foil packs of 28 tablets.

6.6 Special precautions for disposal and other handling

No special requirements. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

AstraZeneca UK Limited,

1 Francis Crick Avenue,

Cambridge, CB2 0AA, UK.

8. MARKETING AUTHORISATION NUMBER(S)

11377/R1

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

2026 August 22

10. DATE OF REVISION OF THE TEXT

2026 August 22