CASODEX® 50 mg

bicalutamide

Film-coated tablets

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, List of excipients.

Pharmaceutical form

White film-coated tablet

Therapeutic indication

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

Posology and method of administration

Adults

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.

Children

CASODEX is contraindicated in children (see *Contraindications*).

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 *Special warnings and precautions for use*).

Contraindications

CASODEX is contraindicated in females and children (see section *Fertility, pregnancy and lactation*).

CASODEX must not be given to any patient who has shown a hypersensitivity reaction to the active substance or to any of the excipients of this product.

Co-administration of terfenadine, astemizole or cisapride with CASODEX is contraindicated (see section *Interaction with other medicinal products and other forms of interaction*).

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 *Undesirable effects*). 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 (CYP 3A4), as such caution should be exercised when co-administered with drugs metabolised predominantly by CYP 3A4 (see sections *Contraindications* and *Interaction with other medicinal products and other forms of interaction*).

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, although a causal association has not been established with CASODEX. 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 Interaction with other medicinal products and other forms of interaction) 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 Interaction with other medicinal products and other forms of interaction & Undesirable effects).

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 *Contraindications*) and caution should be exercised with the co-administration of CASODEX with compounds such as cyclosporin 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 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 effects 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 anticoagulants dose considered (see sections Special warnings and precautions for use & Undesirable effects).

Fertility, pregnancy and lactation

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

Breast-feeding
Bicalutamide is contraindicated during breastfeeding.

Fertility
Reversible impairment of male fertility has been observed in animal studies (see section Preclinical safety data). A period of subfertility or infertility should be assumed in man.

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.

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 disorder	Very common	Anaemia
Immune system disorder	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 failure[4]
	Not known	QT Prolongation (*see Sections Special warnings and precautions for use and Interaction with other medicinal products and other forms of interaction)*.
Vascular disorders	Very common	Hot flush
Respiratory, thoracic and mediastinal disorders	Uncommon	Interstitial lung disease[5]. Fatal outcomes have been reported.
Gastrointestinal disorders	Very common	Abdominal pain Constipation Nausea
	Common	Dyspepsia Flatulence
Hepato-biliary disorders	Common	Hepatotoxicity, jaundice, hypertransaminasaemia[1]
	Rare	Hepatic failure[2]. 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 tenderness[3]

	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 randomized 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 Special warnings and precautions for use & Interaction with other medicinal products and other forms of interaction).

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.

Pharmacological properties

Pharmacodynamic properties

Antiandrogen, ATC code L02BB03

Mechanism of action

CASODEX 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 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.

Pharmacokinetic properties

CASODEX 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 CASODEX, the (R)-enantiomer accumulates about 10 fold in plasma as a consequence of its long half-life, which also makes it suitable for once daily dosing.

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. 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.

CASODEX 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 CASODEX 150 mg was 4.9 microgram/ml. The amount of bicalutamide potentially delivered to a female partner during intercourse is low and equates to approximately 0.3 microgram/kg. This is below that required to induce changes in offspring of laboratory animals.

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 off-dose.

List of excipient

Lactose
Sodium Starch Glycolate
Povidone
Magnesium Stearate
Methylhydroxypropylcellulose
Polyethylene Glycol 300
Titanium Dioxide

Special precautions for storage

Do not store above 30°C

Shelf life

5 years

HARUS DENGAN RESEP DOKTER

Pack size
Box, 2 blisters @ 14 film-coated tablets
Reg. No.: DKI1235300117A1

Manufactured by:
Corden Pharma GmbH, Plankstadt, Germany for AstraZeneca UK Limited, United Kingdom

Packed and released by:
AstraZeneca Pharmaceutical Co. Ltd
No. 2 Huangshan Road
Wuxi, Jiangsu – China

Imported by:
PT AstraZeneca Indonesia
Cikarang, Bekasi – Indonesia

Date of revision of the text
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ANGEL Doc.ID: Doc ID-001951805 v13.0

Leaflet Informasi Pasien
CASODEX™ 50 mg tablet salut selaput
Bicalutamide

Bacalah seluruh isi leaflet ini dengan seksama sebelum Anda mulai meminum/menggunakan obat ini.

- Simpan leaflet ini. Anda mungkin perlu membacanya di kemudian hari
- Jika Anda memiliki pertanyaan lebih lanjut, silakan bertanya pada dokter, apoteker atau perawat Anda
- Obat ini diresepkan khusus hannya untuk Anda. Jangan berikan pada orang lain. Obat ini dapat membahayakan mereka walaupun tanda-tanda penyakit yang mereka miliki sama dengan Anda
- Jika Anda mengalami efek samping, beritahu dokter, apoteker, ataupun perawat Anda. Hal ini termasuk efek samping yang mungkin terjadi terdapat pada leaflet ini (*lihat bagian 4*)

Leaflet ini berisi informasi mengenai

1. CASODEX 50 MG dan kegunaannya

CASODEX 50 MG termasuk dalam golongan obat anti-androgen, yaitu golongan obat yang dapat memengaruhi beberapa aktivitas androgen (hormon seks pria) di dalam tubuh.
CASODEX 50 MG digunakan untuk mengobati kanker prostat stadium lanjut. Penggunaan CASODEX 50 MG dikombinasikan dengan terapi hormonal atau setelah operasi.

2. Hal yang perlu diketahui sebelum menggunakan CASODEX 50 MG

Jangan mengonsumsi CASODEX 50 MG
Jangan mengonsumsi CASODEX 50 MG jika Anda alergi terhadap Bicalutamide atau bahan lain yang terkandung dalam CASODEX 50 MG.
CASODEX 50 MG tidak boleh dikonsumsi oleh wanita dan anak-anak.
Jangan mengonsumsi CASODEX 50 mg jika Anda sedang mengonsumsi cisapride atau obat golongan anti-histamin tertentu (terfenadine atau astemizole)

Peringatan dan Perhatian

- Jika Anda menderita gangguan atau penyakit yang mempengaruhi organ hati Anda.
- Jika Anda mengalami kondisi berikut: gangguan pada jantung atau pembuluh darah, termasuk masalah irama jantung (aritmia), atau sedang dirawat dengan obat-obatan untuk kondisi ini. Risiko masalah irama jantung dapat meningkat pada pasien yang menggunakan CASODEX 50 MG.
- Jika Anda sedang mengonsumsi obat-obatan lain termasuk yang Anda beli sendiri. Khususnya jika Anda sedang mengonsumsi obat pengencer darah atau obat untuk mencegah pembekuan darah.
- Jika Anda menderita diabetes.
- Jika Anda mengonsumsi CASODEX 50 MG, Anda dan/atau pasangan Anda harus menggunakan alat kontrasepsi selama mengonsumsi CASODEX 50 MG dan selama 130 hari setelah berhenti mengonsumsi CASODEX 50 MG. Bicaralah dengan dokter Anda jika Anda memiliki pertanyaan tentang kontrol kelahiran.

Jika Anda ke rumah sakit, beritahu staf medis bahwa Anda sedang mengonsumsi CASODEX 50 MG. Penghentian konsumsi tablet hanya jika sesuai anjuran dokter.

Kehamilan, menyusui, dan kesuburan
CASODEX 50 MG tidak boleh digunakan oleh wanita, termasuk wanita hamil atau ibu yang sedang menyusui bayinya.

CASODEX 50 MG dapat memengaruhi kesuburan pria tetapi tidak permanen.

Mengemudi dan menjalankan mesin
CASODEX 50 MG dapat membuat Anda mengantuk sehingga Anda harus berhati-hati saat mengemudi atau menggunakan mesin.

Informasi penting terkait bahan lain yang terdapat di dalam CASODEX 50 MG
Tablet salut selaput CASODEX 50 MG mengandung laktosa dan titanium dioksida, yang dapat menyebabkan masalah pada sejumlah kecil pasien yang sensitif terhadapnya.

Menggunakan obat-obatan lainnya
Harap beri tahu dokter Anda jika Anda sedang atau baru saja mengonsumsi obat lain, termasuk obat yang tidak diresepkan.
- Khususnya, harap beri tahu dokter Anda jika Anda mengonsumsi pengencer darah seperti warfarin
- CASODEX 50 MG dapat mengganggu beberapa obat yang digunakan untuk mengobati masalah irama jantung atau mungkin meningkatkan risiko masalah irama jantung bila digunakan dengan obat lain yang dapat menyebabkan kelainan irama jantung.
- Harap beri tahu dokter atau apoteker Anda apabila Anda sedang dalam pengobatan menggunakan
    - Obat Siklosporin (untuk menekan sistem kekebalan tubuh)
    - Obat penghambat kanal kalsium (untuk mengobati kondisi tekanan darah tinggi

atau kondisi gangguan jantung)
- Obat simetidin (untuk mengobati masalah lambung)
- Obat Ketokonazol (untuk mengobati infeksi yang disebabkan oleh jamur)

Harap dicatat bahwa pernyataan ini mungkin juga berlaku untuk produk yang digunakan beberapa waktu lalu.

3. Cara Penggunaan CASODEX 50 MG

- Selalu minum CASODEX 50 MG tepat seperti instruksi dokter Anda.
- Dosis dewasa umumnya adalah satu tablet CASODEX 50 mg sehari.
- Telan satu tablet utuh sambil minum air.
- Usahakan meminum tablet di waktu yang sama setiap hari.

Jika Anda menggunakan CASODEX 50 MG lebih dari yang seharusnya

Jika Anda mungkin telah mengonsumsi/menggunakan CASODEX 50 MG lebih banyak dari yang seharusnya, hubungi dokter Anda atau rumah sakit terdekat.

Jika Anda lupa meminum obat

Jika Anda melewatkan satu dosis, jangan menggunakan dosis tambahan, lanjutkan menggunakan seperti biasa.

4. Efek Samping yang Mungkin Terjadi

Seperti semua obat-obatan, CASODEX 50 MG dapat memiliki efek samping.
Segera hubungi dokter atau cari pertolongan medis jika mengalami hal-hal berikut:

- Sesak napas berat, atau sesak napas yang memburuk secara tiba-tiba, yang mungkin disertai batuk atau demam. Beberapa pasien yang mengonsumsi CASODEX 50 mg mengalami radang paru-paru yang disebut penyakit paru interstisial.
- Gatal parah pada kulit (permukaan kulit menonjol) atau pembengkakan pada wajah, bibir, lidah, dan/atau tenggorokan, yang dapat menyebabkan kesulitan menelan.
- Darah dalam urin
- Nyeri perut
- Mata dan kulit kuning (*jaundice*). Ini mungkin gejala kerusakan lever.

Beri tahu dokter sesegera mungkin jika salah satu efek samping berikut mengganggu Anda:

- Jaringan payudara lunak atau membesar
- Muka memerah
- Mual
- Gatal
- Letih
- Pusing
- Ruam
- Kulit kering
- Nyeri dada

- Kehilangan nafsu makan
- Gairah seks berkurang
- Impotensi
- Depresi
- Kantuk
- Gangguan pencernaan
- Perut kembung/flatulensi
- Rambut rontok atau tidak tumbuh lagi
- Penambahan berat badan
- Bengkak
- Penurunan fungsi jantung, atau serangan jantung
- Peningkatan sensitivitas kulit terhadap sinar matahari

Terkadang, CASODEX 50 MG dapat dikaitkan dengan perubahan dalam darah Anda yang mungkin mengharuskan dokter untuk melakukan tes darah tertentu.
Jangan khawatir dengan daftar kemungkinan kejadian tersebut. Anda mungkin tidak mengalami apa pun.

5. Cara Penyimpanan CASODEX 50 MG

Jauhkan dari jangkauan dan pandangan anak-anak.
Jangan disimpan di atas suhu 30ºC.
Simpan di dalam kemasan aslinya.
Jika dokter memutuskan untuk menghentikan pengobatan Anda, buang tablet dengan cara yang tepat.
Gunakan sebelum tanggal: Jangan gunakan CASODEX 50 MG setelah lewat tanggal kedaluwarsa yang tercantum pada kemasan.
Ingatlah untuk mengembalikan tablet yang tidak digunakan ke apoteker.

6. Isi Kemasan dan Informasi Lainnya

CASODEX 50 MG mengandung:
Zat aktif Bicalutamide. Setiap tablet salut selaput CASODEX 50 mg mengandung Bicalutamide 50 miligram

Bahan lainnya adalah laktosa monohidrat, natrium pati glikolat, povidon, magnesium stearat, metilhidroksipropilselulosa, polietilen glikol 300, dan titanium dioksida.

CASODEX 50 MG dikemas dalam karton berisi 2 blister, masing-masing terdiri dari 14 tablet salut selaput.

HARUS DENGAN RESEP DOKTER
Diproduksi oleh:

Corden Pharma GmbH, Plankstadt, Germany
untuk AstraZeneca UK Limited, United Kingdom

Dikemas dan Dirilis oleh:
AstraZeneca Pharmaceutical Co. Ltd
No.2 Huangshan Road
Wuxi, Jiangsu – China

Diimpor oleh:
PT AstraZeneca Indonesia
Cikarang, Bekasi – Indonesia

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