160x270mm
Pantone 655C

2028

Androdex® 50mg

(Bicalutamide)
Film coated tablets

Composition
Each film coated tablet contains 50 mg Bicalutamide.
Excipients: Lactose monohydrate, sodium starch glycolate type A, povidone K-30, purified water, magnesium stearate, hypromellose E5, titanium dioxide, macrogol 400.

Pharmaceutical form
White to off white, round, biconvex, film-coated tablet.

Therapeutic Indications
Treatment of advanced prostate cancer in combination with LHRH analogue therapy or surgical castration.

Posology and method of administration
- Adult males including the elderly: one tablet (50 mg) once a day. Treatment with **Androdex** should be started at the same time as treatment with an LHRH analogue or surgical castration.
- Children: **Androdex** is contraindicated 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: Warnings & precautions for use).

Contraindications
- Bicalutamide is contraindicated 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 contraindicated.

Warnings & 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, **Androdex** 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 (see: Undesirable effects). Bicalutamide therapy should be discontinued if changes are severe.
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: Contraindications and Interactions).

Each tablet of Androdex contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Interactions
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 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 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 **Androdex** 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.

Pregnancy and Lactation
Bicalutamide is contraindicated in females and must not be given to pregnant women or nursing mothers.

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.

Undesirable effects
Bicalutamide in general, has been well tolerated with few withdrawals due to adverse events.

Frequency of Adverse Reactions

43.275 px	System Organ Class	Event
Very common (≥10%)	Reproductive system and breast disorders	Breast tenderness[1] Gynaecomastia[1]
	General disorders	Hot flushes
Common (≥ 1% and < 10%)	Gastrointestinal disorders	Diarrhoea Nausea
	Hepato-biliary disorders	Hepatic changes (elevated levels of transaminases, cholestasis and jaundice)[2]
	General disorders	Asthenia Pruritus

Uncommon (≥ 0.1% and < 1%)	Immune system disorders	Hypersensitivity reactions, including angioneurotic oedema and urticaria
	Respiratory, thoracic and mediastinal disorders	Interstitial lung disease
Rare (≥ 0.01% and < 0.1%)	Gastrointestinal disorders	Vomiting
	Skin and subcutaneous tissue disorders	Dry skin
	Hepato-biliary disorders	Hepatic failure

1. May be reduced by concomitant castration.
2. Hepatic changes are rarely severe and were frequently transient, resolving or improving with continued therapy or following cessation of therapy (see: warnings and precautions for use).

Rare cardiovascular effects such as angina, heart failure, conduction defects including PR and QT interval prolongations, arrhythmias and non-specific ECG changes have been observed. Thrombocytopenia has been reported uncommonly.

In addition, the following adverse experiences were reported in clinical trials (as possible adverse drug reactions in the opinion of investigating clinicians, with a frequency of ≥ 1%) during treatment with Bicalutamide plus an LHRH analogue. No causal relationship of these experiences to drug treatment has been made and some of the experiences reported are those that commonly occur in elderly patients:

Cardiovascular system: heart failure.

Gastrointestinal system: anorexia, dry mouth, dyspepsia, constipation, flatulence.

Central nervous system: dizziness, insomnia, somnolence, decreased libido.

Respiratory system: dyspnoea.

Urogenital: impotence, nocturia.

Haematological: anaemia.

Skin and appendages: alopecia, rash, sweating, hirsutism.

Metabolic and nutritional: diabetes mellitus, hyperglycaemia, oedema, weight gain, weight loss.

Whole body: abdominal pain, chest pain, headache, pain, pelvic pain, chills.

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.

Pharmacological properties

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.

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 9µg per 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 metabolized (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.

Preclinical safety data

Bicalutamide is a potent anti-androgen and a mixed function oxidase enzyme inducer in animals. Target organ changes, including tumour induction, in animals, are related to these activities. Enzyme induction has not been observed in man. None of the findings in the preclinical testing is considered to have relevance to the treatment of advanced prostate cancer patients.

Pharmaceutical particulars

Incompatibilities

None known.

Shelf life

Please refer to expiry date on the blister strip or outer carton.

Precautions for storage

Store below 30°C.

Instructions for use, handling and disposal

No special precautions required.

Pack size

28 and 30 film coated tablets per pack.

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This is a medicament

- A medicament is a product that affects your health, and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are experts in medicine, its benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your doctor.
- Keep out of reach of children.

Council of Arab Health Ministers
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Al Taqaddom Pharmaceutical Industries,
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