Summary of Product Characteristics (SPC)

1. Name of the medicinal product

BICATERO 50 (Bicalutamide Tablets 50 mg)

2. Qualitative and quantitative composition

White colored, round shaped, biconvex film coated tablets, debossed with **2** on one side and **H** on the other side.

3. Pharmaceutical form

Film-coated tablet

4. Clinical particulars

4.1 Therapeutic indications

Treatment of advanced prostate cancer in combination with Luteinising Hormone-Releasing Hormone (LHRH) analogue therapy or surgical castration.

4.2 Posology and method of administration

Adult males including the elderly : one tablet (50 mg) once a day.
Treatment with BICATERO 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
BICATERO is contraindicated for use in children (see section 4.6).

4.3 Contraindications

- BICATERO is contraindicated in women 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 BICATERO is contra-indicated (see section 4.5).

4.4 Special warnings and precautions for use

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

BICATERO 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 BICATERO. Therefore, BICATERO should be used with caution in patients with moderate to severe hepatic impairment.

Periodic liver function testing should be considered due to possibility of hepatic changes. The majority of changes are expected to occur within the first 6 months of BICATERO therapy.

Severe hepatic changes and hepatic failure have been observed rarely with BICATERO, and fatal outcomes have been reported (see section 4.8). BICATERO 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 BICATERO in combination with LHRH agonists.

BICATERO 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).

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

<u>Androgen deprivation therapy may prolong the QT interval</u>

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 BICATERO.

Antiandrogen therapy may cause morphological changes in spermatozoa. Although the effect of BICATERO on sperm morphology

has not been evaluated and no such changes have been reported for patients who received BICATERO, patients and/or their partners should follow adequate contraception during and for 130 days after BICATERO therapy.

Potentiation of coumarin anticoagulant effects have been reported in patients receiving concomitant BICATERO 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).

4.5 Interaction with other medicinal products and other forms of interaction

There is no evidence of any pharmacodynamic or pharmacokinetic interactions between BICATERO and LHRH analogues.

In vitro studies have shown that the (R)-enantiomer of BICATERO 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 BICATERO, mean midazolam exposure (AUC) was increased by up to 80 %, after co-administration of BICATERO 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 BICATERO 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 BICATERO therapy.

Caution should be exercised when administering BICATERO to patients taking medicinal products that inhibit the oxidation processes in the liver, e.g. cimetidine and ketoconazole. This could result in increased plasma concentrations of BICATERO which theoretically could lead to an increase in side effects.

In vitro studies have shown that BICATERO 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 BICATERO. It is therefore

recommended that if BICATERO 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 BICATERO 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.

4.6 Fertility, pregnancy and lactation

Pregnancy

BICATERO is contraindicated in females and must not be given to pregnant women. Breast-feeding
BICATERO 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

BICATERO is unlikely to impair the ability of patients to drive or operate machinery. However, it should be noted that occasionally dizziness or somnolence may occur (see section 4.8). 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).

System Organ Class	**Frequency**	**Undesirable effect**
Blood and the lymphatic	Very Common	Anaemia

system disorders		
Immune system disorders	Uncommon	Hypersensitivity Angioedema Urticaria
Metabolism and nutrition disorders	Common	Decreased appetite
Psychiatric disorders	Common	Decreased libido Depression
Nervous system disorders	Common	Dizziness Somnolence
Cardiac disorders	Common	Myocardial infarction (fatal outcomes
	Not known	have been reported), cardiac failure
Vascular disorders	Very Common	Hot flush
Respiratory, thoracic and mediastinal disorders	Uncommon	Interstitial lung disease1 (fatal outcomes have been reported)
Gastrointestinal disorders	Very Common	Abdominal pain Constipation Nausea
	Common	Dyspepsia Flatulence
Hepato-biliary disorders	Common	Hepatotoxicity Jaundice Hypertransaminasaemia 2
	Rare	Hepatic failure3 (fatal outcomes have been reported)
Skin and subcutaneous tissue disorders	Common	Rash Alopecia
		Hirsutism/hair growth Dry skin Pruritis
		Hirsutism/hair growth Dry skin Pruritis
	Rare	Photosensitivity reaction
Renal and urinary disorders	Very Common	Haematuria

Reproductive system and breast disorders	Very common	Gynaecomastia and breast tenderness5
	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 BICATERO 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 BICATERO 50 mg was used in combination with LHRH agonists, but no increase in risk was evident when BICATERO 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 BICATERO have been reported in post marketing surveillance (see sections 4.4. and 4.5).

Reporting of suspected adverse reactions

Healthcare professionals are requested to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance

Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

1.1 Overdose

There is no human experience of overdosage. There is no specific antidote; treatment should be symptomatic. Dialysis may not be helpful, since BICATERO is highly protein bound and is not recovered unchanged in the urine. General supportive care, including frequent monitoring of vital signs, is indicated.

2. Pharmacological properties

2.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anti-androgen

ATC code: L02BB03

Mechanism of action

BICATERO is a non-steroidal anti-androgen, devoid of other endocrine activity. It binds to the androgen receptors without activating gene expression, and thus inhibits the androgen stimulus. Regression of prostatic tumours results from this inhibition. Clinically discontinuation of BICATERO can result in the "anti-androgen withdrawal syndrome" in a sub-set of patients.

BICATERO is a racemate with its anti-androgenic activity being almost exclusively associated with the (R)-enantiomer

2.2 Pharmacokinetic properties

Absorption

BICATERO is well absorbed following oral administration. There is no evidence of any clinically relevant effect of food on bioavailability.

Distribution

BICATERO 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.

Biotransformation

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 BICATERO, 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 BICATERO. 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-BICATERO in semen of men receiving BICATERO 150 mg was 4.9 microgram/ml. The amount of BICATERO 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

5. BICATERO 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. Pharmaceutical particulars

6. Pharmaceutical particulars

6.1 List of excipients

Lactose monohydrate, Povidone, Crospovidone (type A), Magnesium

stearate, Opadry white-Y-1-7000.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 Months

6.4 Special precautions for storage

Store below 30°C and protect from moisture.

6.5 Nature and contents of container

30's HDPE Container & 10's Blister pack (Alu-PVC)

6.6 Special precautions for disposal and other handling

No special requirements

7.Marketing authorization holder and manufacturing site addresses

Hetero Labs Limited
HETEROCORPORATE 7-2-A2,Industrial Estates,
Sanath Nagar Hydeabad-500 018 Telangana,India

8.Marketing authorization number

H2016/CTD1461/597

9.Date of first registration / renewal of the registration

25/02/2026

10.Date of revision of the text

25/02/2026