BICAMIDE

BICALUTAMIDE

F.C. TABS 50mg/tab

Name of the medicinal product: Bicamide

Composition: Active substance: Bicalutamide. Excipients: Lactose monohydrate, Povidone K-25, Sodium starch glycollate, Magnesium stearate, Hypromellose, Titanium dioxide, Propylene glycol.

Pharmaceutical form: Film coated tablets.

Content in active substance: Each tablet contains 50mg of Bicalutamide.

Description – Packaging: Box that contains 2 blisters of 14 tablets each.

Pharmacotherapeutic group: Hormone andagonists and related agents (Anti-androgens).

Marketing Authorization Holder : GENEPHARM SA. 18th km., Marathon Avenue, 153 51 Pallini, Attica-Greece

Manufacturer: GENEPHARM SA., 18th km., Marathon Avenue, 153 51 Pallini, Attica-Greece

WHAT YOU SHOULD KNOW ABOUT THE DRUG PRESCRIBED TO YOU BY YOUR DOCTOR.

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

Contraindications: Bicamide is contra-indicated in females and children.

Bicamide must not be given to any patient who has shown a hypersensitivity reaction to its use.

Co-administration of terfenadine, astemizole or cisapride with Bicamide is contra-indicated.

Special warnings and precautions for use

General: Bicamide 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 Bicamide. Therefore, Bicamide 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 Bicamide therapy. Severe hepatic changes have been observed rarely with Bicamide. Bicamide therapy should be discontinued if changes are severe. Bicamide 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.

Pregnancy and lactation: Bicamide is contra-indicated in females and must not be given to pregnant women or nursing mothers.

Effect on the ability to **drive and use machines:** Bicamide 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.

Incompatibilities

None reported.

Drug interaction with other medicinal products and other forms of interaction

There is no evidence of any pharmacodynamic or pharmacokinetic interactions between Bicamide 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 Bicamide, mean midazolam exposure (AUC) was increased by up to 80%, after co-administration of Bicamide 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 Bicamide 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 Bicamide therapy. Caution should be exercised when prescribing Bicamide with other drugs which may inhibit drug oxidation e.g. cimetidine and ketoconazole. In theory, this could result in increased plasma concentrations of Bicamide which theoretically could lead to an increase in side effects.

In vitro studies have shown that Bicamide can displace the coumarin anticoagulant, warfarin, from its protein binding sites. It is therefore recommended that if Bicamide is started in patients who are already receiving coumarin anticoagulants, prothrombin time should be closely monitored.

Dosage and administration :Adult males including the elderly: one tablet (50mg) once a day. Treatment with Bicamide should be started at least 3 days before commencing treatment with an LHRH analogue, or at the same time as surgical castration.
Children: Bicamide is contra-indicated 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.

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

Undesirable effects :Bicamide in general, has been well tolerated with few withdrawals due to adverse events.
May be reduced by concomitant castration.
Hepatic changes are rarely severe and were frequently transient, resolving or improving with continued therapy or following cessation of therapy.
Hepatic failure has occurred very rarely in patients treated with Bicamide, but a causal relationship has not been established with certainty. Periodic liver function testing should be considered.
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 rarely.
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 $\geq$ 1%) during treatment with Bicamide 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.

Missed dose: Not applicable

Shelf- life:It is printed on the inner and outer package. If the date has expired do not use the medicine.

Storage:Store at temperature below 25°C, out of the reach of children.

INFORMATION ON THE RATIONAL USE OF MEDICINES

- This drug was prescribed to you by your doctor only for your specific medical problem. You should not give it to other people or use it for any other disease without first consulting your doctor.
- If any problem with the medicine is experienced during the treatment, tell your doctor or your pharmacist immediately.
- If you have any questions regarding the information concerning the medicine you are taking or if you need to be better informed about your medical problem, do not hesitate to request this information from your doctor or your pharmacist.
- In order for the drug that has been prescribed to you to be effective and safe, it must be taken according to the instructions given to you.
- For your safety and good health, it is necessary to read carefully any information concerning the medicine that was administered to you.
- Do not keep medicines in bathroom cabinets, because heat and humidity may spoil the medicine and render it harmful for your health.
- Do not keep medicines that you do not need any more or that have already expired.
- For increased safety, keep all medicines in a safe place away from children.

This medicine is given only under physician's prescription.