PROFESSIONAL INFORMATION FOR HUMAN MEDICINES

SCHEDULING STATUS S4

1 NAME OF THE MEDICINE

Caloxa 50 mg (Film coated tablets)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 50 mg bicalutamide.

Excipients with known effect:

Contains sugar (Lactose)

Each tablet contains 56 mg lactose monohydrate.

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Film coated tablets

White to off-white, round, biconvex, film coated tablets debossed ‘B 50’ on one side and plain on other side.

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 Caloxa 50 mg should be started at least three days before commencing treatment with a 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).

4.3 Contraindications

Females and children, pregnant women or breastfeeding mothers.

Caloxa 50 mg must not be given to any patient who has shown a hypersensitivity reaction to its use.

4.4 Special warnings and precautions for use

Hepatic function impairment:

Caloxa 50 mg 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 Caloxa 50 mg.

Metabolism of Caloxa 50 mg may be delayed in patients with moderate to severe hepatic function impairment, resulting in a prolonged elimination half-life and increased risk of toxicity. Therefore, Caloxa 50 mg should be used with caution in patients with moderate to severe hepatic impairment.

Periodic liver function testing should be considered during long-term use of Caloxa 50 mg, due to the possibility of hepatic changes. Severe hepatic changes have been observed infrequently

with Caloxa 50 mg (see section 4.8). Caloxa 50 mg therapy should be discontinued if changes are severe.

Medicines metabolised by cytochrome P450:

Although clinical studies using antipyrine as a marker of Cytochrome P450 (CYP) activity showed no evidence of a drug interaction potential with Caloxa 50 mg, midazolam exposure (AUC) was increased by up to 80 %, after co-administration with Caloxa 50 mg for 28 days. This rise is comparable to that seen in other studies after administration of grapefruit juice. Caution should be exercised with the co-administration of Caloxa 50 mg with compounds such as these.

4.5 Interactions with other medicines and other forms of interaction

Luteinising Hormone Releasing Hormone (LHRH):

There is no evidence of any pharmacodynamic or pharmacokinetic interactions between Caloxa 50 mg and LHRH analogues.

Ketoconazole and Cimetidine:

Formal interaction studies have not been undertaken, but caution should be exercised when prescribing Caloxa 50 mg with other medicines, e.g. ketoconazole and cimetidine, which may

inhibit oxidation of Caloxa 50 mg. It could result in increased plasma concentrations of Caloxa 50 mg which could lead to an increase in side-effects.

Medicines Metabolised by Cytochrome P450:

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Coumarin Anticoagulants:

Caloxa 50 mg can displace the coumarin anticoagulant, warfarin, from its protein binding sites. It is therefore recommended that if Caloxa 50 mg is started in patients who are already receiving coumarin anticoagulants, prothrombin time should be closely monitored.

4.6 Fertility, pregnancy and lactation

Safety and efficacy of Caloxa 50 mg during pregnancy and lactation have not been established, (see section 4.3).

4.7 Effects on ability to drive and use machines

During treatment with Bicalutamide, somnolence has been reported and those patients who experience this symptom should not drive or use machines.

4.8 Undesirable effects

Blood and lymphatic system disorders

Frequent: Anaemia

The following side effects have been reported but the frequencies are unknown: Leucopenia, neutropenia, thrombocytopenia

Immune system disorders

Less frequent: Hypersensitivity reactions (including angioneurotic oedema and urticaria)

Metabolism and nutrition disorders

Frequent: Anorexia, decreased appetite

The following side effects have been reported but the frequencies are unknown: Diabetes mellitus, hyperglycaemia.

Psychiatric disorders

Frequent: depression, decreased libido

Nervous system disorders

Frequent: Dizziness, somnolence, insomnia

Less frequent: Reversible neurological reactions such as nervousness, drowsiness and confusion

Cardiac disorders

Frequent: Myocardial infarction (fatal outcomes have been reported), cardiac failure

Vascular disorders

Frequent: Hypertension, Hot flush

Respiratory, thoracic and mediastinal disorders

Frequent: Upper respiratory tract infection, cough or hoarseness, shortness of breath, sore throat and sneezing

Less frequent: Interstitial lung disease and dyspnoea. Fatal outcomes have been reported.

Gastrointestinal disorders

Frequent: Abdominal pain, constipation, nausea, dyspepsia, flatulence, diarrhoea

Less frequent: Gastro-intestinal or rectal bleeding, vomiting

Hepato-biliary disorders

Frequent: Hepatic changes (including elevated levels of transaminases, jaundice), hepatitis

Less frequent: Hepatic failure.

The following side effects have been reported but the frequencies are unknown:

Methaemoglobinaemia

Skin and subcutaneous tissue disorders

Frequent: Alopecia, hirsuitism/hair re-growth, dry skin, pruritis, rash, sweating

Renal and urinary disorders

Frequent: Haematuria

The following side effects have been reported but the frequencies are unknown: Nocturia

Reproductive system and breast disorders

Frequent: Gynaecomastia and breast tenderness, impotence, decreased libido, erectile dysfunction

General disorders and administration site conditions

Frequent: Asthenia, oedema, chest pain, fever, chills, flu-like syndrome

Investigations

Frequent: Weight gain

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

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 Caloxa 50 mg 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

A 21.12 Hormone inhibitors

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. Bicalutamide is a racemate with its anti-androgenic activity being almost exclusively in the (R) - enantiomer. Bicalutamide is an anti-androgen and a mixed function oxidase enzyme inducer in animals. Target organ changes, including tumour induction, in animals, are related to these activities. None of the findings in the preclinical testing is considered to have relevance to the treatment of advanced prostate cancer patients.

5.2 Pharmacokinetic properties

Bicalutamide is highly plasma protein bound and extensively metabolised (via oxidation and glucuronidation); Its metabolites are eliminated via the kidneys and bile in approximately equal portions.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hypromellose

Lactose monohydrate

Macrogol 400

Magnesium stearate

Povidone

Sodium starch glycolate

Titanium dioxide

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store at or below 25 °C. Store in original package.

6.5 Nature and contents of container

Caloxa 50 mg Tablets: 10 tablets per Clear PVC / PVdC-Aluminium blister strip, supplied in a pack size of 30.

6.6 Special precautions for disposal

No special requirements

7 HOLDER OF CERTIFICATE OF REGISTRATION

Eurolab (Pty) Ltd.

Woodmead Office Park

3 Stirrup Lane, Van Reenans Avenue

Woodmead

Gauteng

South Africa

8 REGISTRATION NUMBER

42/21.12/0430

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

26 November 2010

5 February 2015

10 DATE OF REVISION OF THE TEXT

31 January 2023