Ministry of Health, Welfare and Sport
CIBG
P.O. Box 16114
2500 BC Den Haag
The Netherlands

Certificate of a Pharmaceutical Product[1]

This certificate conforms to the format recommended by the World Health Organization.
(Explanatory Notes and General Instructions attached)

Exporting (certifying) country: **The Netherlands** No. of Certificate: 21-01471

Importing (requesting) country: **Chile**

1. Name and dosage form of product

Name in the Netherlands: Biluron 150 mg, filmomhulde tabletten
Dosage form: Film-coated tablets
Legal status: POM

Name in Chile: Biolev comprimidos recubiertos 150 mg

1.1 Active ingredient(s)[2] and amount(s) per unit dose[3].
150.0 mg Bicalutamide per film-coated tablet
For complete composition including excipients see appendix 1 of this certificate.

1.2 Is this product licensed to be placed on the market for use in The Netherlands?[4]

(a) yes/no **YES**
(b) application pending: yes/no **NO**

1.3 Is this product on the market in The Netherlands? yes/no/unknown **YES**

2A.1 Number of product licence[6] and date of issue:
RVG 102251, 03-11-2009

2A.2 Product licence holder (name and address):

Genthon BV
Microweg 22
6545 CM Nijmegen
The Netherlands

2A.3 Status of product licence holder[7] : a/ b/ c/ **C**

2A.3.1 For categories b and c the name and address of the manufacturer producing the dosage form is:[8]

Synthon Hispania, S.L.
C/Castelló, 1
08830 Sant Boi de Llobregat
Barcelona
Spain
(manufacturing site, packaging site, release testing site, release site)

2A.4 Is summary basis of approval appended?[9] **No**

2A.5 Is officially approved product information, complete and consonent with the licence, attached?
Yes
For approved product information please refer to appendix 2 of this certificate

2A.6 Applicant for certificate, if different from licence holder (name and address)[11]:
Synthon BV
Microweg 22
6545 CM Nijmegen
Netherlands

3. Does the Netherlands' certifying authority arrange for periodic inspection of the manufacturing plant in which the dosage form is produced?

No. The facilities outside the territory of The Netherlands' certifying authority are inspected by the local competent authority.

4. Does the information submitted by the applicant satisfy the Netherlands' certifying authority on all aspects of the manufacture of the product[15].

Yes

.....
.....

Address of certifying authority:
Ministry of Health, Welfare and Sport
CIBG
P.O. Box 16114
2500 BC Den Haag, the Netherlands

Name of authorized person:
.....
dr. M.J. van de Velde, PhD

Signature:
.....

Stamp and date:
.....
11 OKT. 2021

APOSTILLE

(Convention de La Haye du 5 octobre 1961)

1. Country: THE NETHERLANDS
   This public document
2. has been signed by **dr. M.J. van de Velde**
3. acting in the capacity of Registrar of Medical Professions
4. bears the seal/stamp of the Ministry of Health, Welfare and Sport

Certified

5. in Arnhem
6. on 18-10-2021
7. by the registrar of the district court of Gelderland
8. no. 21-2974

9. Seal/stamp:
10. Signature:

C. Boers

3.2.P.1 Description and Composition of the Drug Product

Description of the drug product

White, round, biconvex film-coated tablet. The tablet is debossed with "BCM 150" on one side.

Composition of the drug product

Ingredients	Mass per tablet [mg]	Quality	Function
Core			
Bicalutamide [1]	150.0	DMF	Drug substance
Lactose monohydrate[2]		Ph. Eur.	Diluent
Povidone		USP/NF	Binder
Crospovidone		USP/NF	Disintegrant
Sodium lauryl sulfate [3]		Ph. Eur.	Wetting agent
Magnesium stearate [3]		Ph. Eur.	Lubricant
Purified water [4]		Ph.Eur.	solvent
Total mass			
Lactose monohydrate		Ph. Eur.	Filler
Hypromellose		Ph. Eur.	Film forming agent
Titanium dioxide		Ph. Eur.	Opacifier
Macrogol (PEG 4000)		Ph. Eur.	Plasticizer
Purified water [6]		Ph.Eur.	solvent
Total mass			

[1] Prior to manufacturing a correction factor (F) is calculated by the QA/QC department. The correction factor compensates for assay (HPLC, dry basis) and water content (w.c. , based on loss on drying). Both values are presented on the Certificate of Analysis from Synthon that should accompany each batch of Bicalutamide.

$$F = \frac{100 \times 100}{(100 - \text{w.c. (\%)}) \times \text{assay (\%)}}$$

When the assay of Bicalutamide drug substance (HPLC, dry basis) is >100%, then 100.0 % has to be used in the equation.

[2] Lactose monohydrate is also used to compensate for the mass change of the tablet. The compensation mass (C) is defined as:

$$C = \text{Batch size} \times 0.150 \times [F - 1] \text{ (g)}$$

[3] Prepared from vegetable sources.

[4] Removed during the drying process to a level of <2.0% (based on loss on drying test)

[5] Coating ingredients (except water) are equivalent to a ready-to-use Opadry II OY-L-28900 white coating mixture of the company Colorcon.

[6] Removed during the coating process

Type of closure of the dosage form

The primary packaging material is an opaque PVC/PE/PVDC/Al blister. This blister consists of 250 µm thick PVC foil, 25 µm thick PE foil, with a PVDC coating of 90 g/m^2 welded on an internally film coated 20 µm aluminium semi rigid support.

Laura Rodríguez
Qualified Person

Summary of Product Characteristics - Core

1. NAME OF THE MEDICINAL PRODUCT

<Bicalutamide 150 mg, film-coated tablets>

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 150 mg of bicalutamide

Excipient(s) with known effect
Each tablet contains 181.32 mg lactose monohydrate

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet.

White, round, biconvex, film-coated tablet, debossed with BCM 150 on one side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Bicalutamide 150 mg is indicated either alone or as adjuvant to radical prostatectomy or radiotherapy in patients with locally advanced prostate cancer at high risk for disease progression (see section 5.1).

Bicalutamide 150 mg is also indicated for the management of patients with locally advanced, non-metastatic prostate cancer for whom surgical castration or other medical intervention is not considered appropriate or acceptable.

4.2 Posology and method of administration

Posology
Adult males, including elderly: 150 mg (1 tablet) to be taken orally once per day.

Paediatric population
Bicalutamide is not indicated in children and adolescents.

5.3 Preclinical safety data

Bicalutamide is a potent antiandrogen and a mixed function oxidase enzyme inducer in animals. Target organ changes, including tumour induction (Leydig cells, thyroid, liver) in animals, are related to these activities.. Enzyme induction has not been observed in man and none of these findings is considered to have relevance to the treatment of patients with prostate cancer. Atrophy of seminiferous tubules is a predicted class effect with antiandrogens and has been observed for all species examined. Full reversal of testicular atrophy was 24 weeks after a 12 month repeated dose toxicity study in rats, although functional reversal was evident in reproduction studies 7 weeks after the end of an 11 week dosing period. A period of subfertility or infertility should be assumed in man.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:
Lactose monohydrate
Povidone K-29/32
Crospovidone
Sodium laurilsulfate
Magnesium stearate

Coating:
Lactose monohydrate
Hypromellose
Titanium dioxide (E 171)
Macrogol 4,000

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

5 years.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

PVC/PE/PVDC/Al blister pack, box.

Genthon

Appendix 3

To whom it may concern

CERTIFICATE OF PHARMACEUTICAL PRODUCT

Name and dosage form of the product in the Netherlands:
Biluron 150 mg, filmomhulde tabletten

Name and dosage form of the product in English core Summary of Product Characteristics:
Bicalutamide 150 mg, film-coated tablets

The attached Summary of Product Characteristics (SmPC) is the English translation of the current national SmPC approved by the Health Authorities in the Netherlands.

Genthon BV
Marjolijn van der Star
Head Regulatory Affairs Maintenance

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