

**IRISH MEDICINES BOARD ACT 1995**  
**MEDICINAL PRODUCTS(LICENSING AND SALE)REGULATIONS, 1998**  
**(S.I. No.142 of 1998)**

**PPA1328/073/001**

Case No: 2029776

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

**B & S Healthcare**

**Unit 4, Bradfield Road, Ruislip, Middlesex, HA4 0NU, United Kingdom**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

**Campral EC 333 mg Gastro-Resistant Tablets**

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **30/03/2007** until **29/03/2012**.

Signed on behalf of the Irish Medicines Board this

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A person authorised in that behalf by the said Board.

## Part II

### Summary of Product Characteristics

#### 1 NAME OF THE MEDICINAL PRODUCT

Campral EC 333 mg Gastro-resistant tablets.

#### 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gastro-resistant tablet contains 333.0 mg acamprosate calcium.  
For a full list of excipients see section 6.1.

#### 3 PHARMACEUTICAL FORM

Gastro-resistant tablet

*Product imported from The Netherlands and Portugal:*

White coated gastro-resistant tablet marked with '333' on one side

#### 4 CLINICAL PARTICULARS

##### 4.1 Therapeutic Indications

Campral EC is indicated as therapy to maintain abstinence in alcohol dependent patients. It should be combined with counselling.

##### 4.2 Posology and method of administration

*Adults:*

Within the age range 18-65 years:

§ Subjects weighing 60 kg or more:

2 tablets three times daily with meals (2 tablets morning, noon and night).

§ Subjects weighing less than 60 kg:

4 tablets divided into three daily doses with meals (2 tablets in the morning, 1 at noon, 1 at night).

*Children and the Elderly:*

Campral EC should not be administered to children and the elderly.

The recommended treatment period is one year. Treatment with Campral EC should be initiated as soon as possible after the withdrawal period and should be maintained if the patient relapses.

##### 4.3 Contraindications

- in patients with a known hypersensitivity to the drug
- in pregnant women and lactating women

- in cases of renal insufficiency (serum creatinine > 120 micromol/L)
- in cases with severe hepatic failure (Childs- Pugh Classification C)

## 4.4 Special warnings and precautions for use

Campral EC does not constitute treatment for the withdrawal period.

The prescription of the product should be initiated under the direct supervision of a consultant or a clinician experienced in the field, working in a hospital based clinic or an alcohol treatment unit. General practitioners with an interest in treating alcohol dependent patients are allowed to initiate and/or pursue Campral treatment.

## 4.5 Interaction with other medicinal products and other forms of interaction

The concomitant intake of alcohol and Campral EC does not affect the pharmacokinetics of either alcohol or acamprosate. Administering Campral EC with food diminishes the bioavailability of the drug compared with its administration in the fasting state. Pharmacokinetic studies have been completed and show no interaction between acamprosate and diazepam, disulfiram or imipramine. There is no information available on the concomitant administration of Campral EC with diuretics.

## 4.6 Pregnancy and lactation

Although animal studies have not shown any evidence of foetotoxicity or teratogenicity, the safety of acamprosate has not been established in pregnant women. Acamprosate is excreted in the milk of lactating animals and safe use has not been demonstrated in lactating women. Campral EC therefore should not be administered to pregnant or to breast feeding women.

## 4.7 Effects on ability to drive and use machines

Campral EC should not impair the patient's ability to drive or operate machinery.

## 4.8 Undesirable effects

Adverse events associated with Campral EC tend to be mild and transient in nature. They are predominantly gastrointestinal or dermatological. Diarrhoea, and less frequently nausea, vomiting and abdominal pain are the gastrointestinal adverse events. Pruritus is the predominant dermatological adverse event. An occasional maculopapular rash and rare cases of bullous skin reactions have been reported. Fluctuation in libido has been reported by patients receiving Campral EC as well as by patients receiving the placebo.

As this product represents a novel chemical entity, any suspected adverse events/reactions should be reported to the company and the Irish Medicines Board in the usual way.

## 4.9 Overdose

Five cases of overdose associated with acamprosate therapy have been reported in humans, including one patient who ingested 43 g. After gastric lavage all patients had an uneventful recovery. Diarrhoea was observed in two cases. No case of hypercalcaemia was reported in the course of these overdoses. However, should this occur, the patients should be treated for acute hypercalcaemia.

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Acamprosate calcium (calcium acetylhomotaurinate) has a chemical structure similar to that of amino acid neurotransmitters, such as taurine or gamma-amino-butyric acid (GABA), including an acetylation to permit passage across the blood brain barrier. Acamprosate may act by stimulating GABAergic inhibitory neurotransmission and antagonising excitatory amino-acids, particularly glutamic acid.

Animal experimental studies have demonstrated that acamprosate affects alcohol dependence in rats, decreasing the voluntary intake of alcohol without affecting food and total fluid intake.

### 5.2 Pharmacokinetic properties

Acamprosate absorption across the gastrointestinal tract is moderate, slow and sustained and varies substantially from person to person.

Oral absorption shows considerable variability and is usually less than 10% of the ingested drug in the first 24 hours. Food reduces the oral absorption of acamprosate. Steady state levels of acamprosate are achieved by the seventh day of dosing. Acamprosate is not protein bound.

The drug is excreted in the urine and is not significantly metabolised. There is a linear relationship between creatinine clearance values and total apparent plasma clearance, renal clearance and plasma half-life of acamprosate. The pharmacokinetics of acamprosate are not altered by hepatic dysfunction.

### 5.3 Preclinical safety data

In preclinical studies, signs of toxicity are related to the excessive intake of calcium and not acetylhomotaurine. Disorders of phosphorus/calcium metabolism have been observed including diarrhoea, soft tissue calcification, renal and cardiac lesions.

There were no mutagenic or carcinogenic effects, nor any teratogenic or adverse effects on the male or female reproductive systems of animals.

Detailed *in vitro* and *in vivo* research on acamprosate to detect genetic and chromosomal mutations has not produced any evidence of potential genetic toxicity.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Crospovidone

Microcrystalline cellulose

Magnesium silicate

Sodium starch glycolate

Anhydrous colloidal silica

Magnesium stearate

Anionic copolymer methacrylic acid and acrylic acid ethyl ester

Talc

Propylene glycol

### 6.2 Incompatibilities

Not applicable

## 6.3 Shelf Life

The shelf-life expiry date of this product shall be the date shown on the container and outer package of the product on the market in the country of origin.

## 6.4 Special precautions for storage

Do not store above 25°C.

## 6.5 Nature and contents of container

PVC/PVDC aluminium sheets of blisters containing 12 tablets. Sheets of blisters are presented in cartons of 60 or 84 tablets.

Not all pack sizes may be marketed.

## 6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

## 7 Parallel Product Authorisation Holder

B&S Healthcare  
Unit 4  
Bradfield Road  
Ruislip  
Middlesex HA4 0NU  
United Kingdom

## 8 Parallel Product Authorisation Number

PPA 1328/73/1

## 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of First Authorisation 30<sup>th</sup> March 2007

## 10 DATE OF REVISION OF THE TEXT

July 2006