Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Campral EC 333mg Gastro-resistant tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Gastro-Resistant Tablet contains Acamprosate Calcium 333.0 mg.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Gastro-Resistant Tablet
White coated gastro-resistant tablet with '333' engraved 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

Posology

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).

Older people

Campral EC should not be used in older people.

Paediatric population

Campral EC should not be used in children.

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

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- in lactating women (see section 4.6)
- in cases of renal insufficiency (serum creatinine >120 micromol/L)

4.4 Special warnings and precautions for use

The safety and efficacy of Campral has not been established in patients younger than 18 years or older than 65 years. Campral is therefore not recommended for use in these populations.

The safety and efficacy of Campral has not been established in patients with severe liver insufficiency (Childs-Pugh Classification C).

Because the interrelationship between alcohol dependence, depression and suicidality is well- recognised and complex, it is recommended that alcohol-dependent patients, including those treated with acamprosate, be monitored for such symptoms.

This medicine contains less than 1mmol sodium (23mg) per dosage unit, that is to say it is essentially 'sodium free'

Abuse and dependence

Non-clinical studies suggest that acamprosate has little or no abuse potential. No evidence of dependence on acamprosate was found in any clinical study thus demonstrating that acamprosate has no significant dependence potential.

4.5 Interaction with other medicinal products and other forms of interactions

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.

No change in the frequency of clinical and/or biological adverse reactions has been shown when acamprosate is used concomitantly with disulfiram, oxazepam, tetrabamate or meprobamate.

In clinical trials, acamprosate has been safely administered in combination with antidepressants, anxiolytics, hypnotics and sedatives, and non-opioid analgesics.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no adequate data from the use of Campral in pregnant women. Animal studies do not indicate any evidence of foetotoxicity or tetragenicity. Campral must therefore only be used during pregnancy after a careful benefit/risk assessment, when the patient cannot abstain from drinking alcohol without being treated with Campral and when there is consequently a risk of foetotoxicity or teratogenicity due to alcohol.

Breast-feeding
It is known that Campral is excreted in the milk of lactating animals. It is not known whether acamprosate is excreted in human milk. There are no adequate data from the use of acamprosate in infants. Campral must therefore not be used in breastfeeding women.

If a breastfeeding woman cannot abstain from drinking alcohol without being treated with acamprosate, a decision must be made whether to discontinue nursing or to discontinue Campral, taking into account the importance of the medicinal product to the woman.

Fertility
In animal studies, no adverse effects on fertility were observed. Whether or not acamprosate affects the fertility in humans is unknown.

4.7 Effects on ability to drive and use machines

Campral EC has no influence on the ability to drive and use machines.

4.8 Undesirable effects

According to information collected during clinical trials and spontaneous reports since marketing authorisation, the following adverse reactions may occur under treatment with Campral.

The following definitions apply to the frequency terminology used hereafter: very common (≥ 1/10), common (≥ 1/100, < 1/10), uncommon (≥ 1/1,000, < 1/100), rare (≥ 1/10,000, < 1/1,000), very rare (< 1/10,000, including isolated cases), frequency not known (cannot be estimated from the available data)

Gastrointestinal disorders:
Very common: Diarrhoea
Common: Abdominal pain, nausea, vomiting, flatulence

Skin and subcutaneous tissue disorders:
Common: Pruritus, maculo-papular rash
Not known: Vesiculo-bullous eruptions

Immune system disorders:
Very rare: Hypersensitivity reactions including urticaria, angioedema or anaphylactic reactions.

Reproductive system and breast disorders:
Common: Frigidity or impotence.

Psychiatric disorders:
Common: Decreased libido
Uncommon: Increased libido

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via: HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2. Tel: +353 1 6764971; Fax: +353 1 6762517; Website: www.hpra.ie; E-mail: medsafety@hpra.ie

4.9 Overdose

Acute overdose is usually mild. In the reported cases, the only symptom, which can be reasonably related to overdose is diarrhoea. No case of hypercalcaemia has ever been reported. Treatment of overdose is directed to symptoms.

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 affects 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 Type A
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

3 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/PVDC aluminium sheets of blister containing 12 or 20 tablets. Sheets of blister are presented in cartons of 60, 84 or 200 tablets.

Polypropylene bottles of 125 ml capacity, closed with a tamper-evident polypropylene cap, containing 180 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

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Merck Serono (Ireland) Limited
4045 Kingswood Road
Citywest Business Campus
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER

PA2286/007/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 16 February 1996

Date of last renewal: 05 November 2010

10 DATE OF REVISION OF THE TEXT

December 2020