

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Campral EC

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains acamprosate (I.N.N.) calcium 333.0 mg as the active ingredient.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Enterocoated tablets.

Campral tablets are white and round with '333' engraved on one side and approximately 10 mm in diameter.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Acamprosate 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:

- 2 tablets three times daily with meals (2 tablets morning, noon and night) in subjects weighing 60kg or more.

- In subjects weighing less than 60kg, 4 tablets divided into three daily doses with meals (2 tablets in the morning, 1 at noon and 1 at night).

Older people

Acamprosate should not be used in older people

Paediatric population

Acamprosate should not be used in children

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

Acamprosate does not prevent the harmful effects of continuous alcohol abuse. Continued alcohol abuse negates the therapeutic benefit, therefore acamprosate treatment should only be initiated after weaning therapy, once the patient is abstinent from alcohol.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- 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.

Excipients:

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 interaction

The concomitant intake of alcohol and acamprosate does not affect the pharmacokinetics of either alcohol or acamprosate. Administering acamprosate with food diminishes the bioavailability of the drug compared with its administration in the fasting state.

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

Pharmacokinetic studies have been completed and show no interaction between acamprosate and diazepam, disulfiram, oxazepam, tetrabamate, meprobamate or imipramine.

There is no information available on the concomitant administration of acamprosate with diuretics.

4.6 Fertility, Pregnancy and lactation

Pregnancy

There is 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 acamprosate 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 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 authorization, the following adverse reactions may occur under treatment with Campral.

The following definitions apply to the frequency terminology used hereafter: very common ($\geq 1/10$), common ($\geq 1/100$, $< 1/10$), uncommon ($\geq 1/1,000$, $< 1/100$), rare ($\geq 1/10,000$, $< 1/1,000$), 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, angio-oedema 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 the Yellow Card Scheme at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

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 acetylhomotaurinate) has a chemical structure similar to that of amino-acid neuromediators, 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 glutamate.

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. 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.

Oral absorption shows considerable variability and is usually less than 10% of the ingested drug in the first 24 hours. The drug is excreted in the urine and is not metabolised significantly. There is a linear relationship between creatinine

clearance values and total apparent plasma clearance, renal clearance and plasma half-life of acamprosate.

The kinetics of acamprosate are not modified in group A or B of the Child-Pugh classification of impaired liver function, a population which is likely to be part of the target population for acamprosate. This is in accordance with the absence of hepatic metabolism of the drug.

5.3 Preclinical safety data

In the preclinical studies, signs of toxicity are related to the excessive intake of calcium and not to acetylhomotaurine. Disorders of phosphorus/calcium metabolism have been observed including diarrhoea, soft tissue calcification, renal and cardiac lesions. Acamprosate had no mutagenic or carcinogenic effect, 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 (KOLLIDON CL)
Microcrystalline cellulose (AVICEL PH 101)
Magnesium silicate (COMPRESSIL)
Sodium starch glycolate (EXPLOTAB)
Anhydrous colloidal silica (AEROSIL 200)
Magnesium stearate
Anionic copolymer of metacrylic acid and acrylic acid ethyl ester (EUDRAGIT L 30 D)
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 blisters containing 12 or 20 tablets. Sheets of blisters are presented in cartons of 60, 84, 168 or 200 tablets.

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

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 Limited
5 New Square
Bedfont Lakes Business Park
Feltham
Middlesex
TW14 8HA
UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 11648/0289

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

18 December 1995 (first authorization)

10 DATE OF REVISION OF THE TEXT

10/12/2020