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ALCOHOLOGY
Update
October 2018

TRANSPARENCY COMMITTEE OPINION SUMMARY

AOTAL (acamprosate), **ESPERAL** (disulfiram), **REVIA** (naltrexone), alcohol dependence products

High clinical benefit in the management of alcohol dependent patients maintained

Main points

- AOTAL, ESPERAL and REVIA are used to maintain abstinence in alcohol-dependent patients in the context of comprehensive management with psychological counselling.
- AOTAL and REVIA are first-line treatments, while ESPERAL is a second-line treatment due to its antabuse effects.
- A meta-analysis failed to show any significant differences between acamprosate and naltrexone in terms of abstinence and relapse.

Therapeutic strategy

- The therapeutic strategy for alcohol dependence consists of two steps. The first step aims to guide the patient to total abstinence (withdrawal) and is frequently conducted in a hospital setting. The second step focuses on maintaining this abstinence for the longest possible time. This period is frequently punctuated by excessive alcohol consumption relapses. The quality of the caregiver-patient relationship is a major component of the treatment pathway.
- Various therapeutic measures are available for treating alcohol dependence. SELINCRO (nalmefene) is intended to reduce consumption. Combined with psychosocial counselling, it represents a therapeutic option in the reduction of alcohol consumption in alcohol-dependent adults with high-risk alcohol consumption, who do not present with any physical symptoms of withdrawal and who do not require immediatewithdrawal. Baclofen is used to treat alcohol-dependent patients (maximum dosage: 80 mg/day) to reduce their alcohol consumption.
- The therapeutic measures used to maintain abstinence are medicinal products, along with non-pharmacological methods (such as motivational interviews, psychotherapy sessions, mindfulness or reformed drinker groups). According to expert opinion, the ability to propose a medicinal treatment helps attract patients to and maintain them in the care system, which is a major issue for maintenance of abstinence.
- Sometimes, using a new treatment serves to re-energise management. The various treatments serve to bolster the patient's motivation and adherence to treatment in the context of prolonged follow-up.
- **Role of the medicinal product in the therapeutic strategy**
  AOTAL, REVIA and ESPERAL have been granted a MA focused on the post-withdrawal maintenance of abstinence. The treatment must be associated with personalised psychological support. The potential benefit of these treatments is dictated by the patient's compliance. Compliance is a specific stake in treatment success.
- AOTAL and REVIA are first-line medicinal treatments. According to expert opinion, AOTAL could be of special benefit for recently withdrawn patients seeking complete and long-term abstinence, while REVIA could be of special benefit for patients with an abstinence goal and for whom the clinician has detected a significant risk of sporadic consumption, in order to reduce the probability that this sporadic consumption could become excessive.
- ESPERAL is an aversive treatment offered to patients motivated to use this medicinal product. According to expert opinion, this medicinal product remains difficult to replace in patients who request it and who are motivated, though in recurrent relapse situations.

Considering:
- the limited efficacy data, that fail to demonstrate any benefit versus placebo, but in light of the limits of these comparisons relative to the special mode of action of disulfiram,

- the advantages and limits inherent to the antabuse effect of disulfiram,
- its tolerance profile marred in particular by liver toxicity and peripheral neuropathies,

ESPERAL is a second-line treatment intended to maintain abstinence in alcohol-dependent patients in the context of comprehensive management with psychological counselling.

Clinical data

- The results of a meta-analysis confirm the efficacy of acamprosate and naltrexone versus placebo in terms of the risk of alcohol consumption relapse and the number days of alcohol abstinence.
  No significant difference in these 2 endpoints was observed between acamprosate and naltrexone.
  No studies have compared acamprosate or naltrexone to disulfiram.
  There are no new pharmacovigilance signals for acamprosate and naltrexone.
- An indirect comparison meta-analysis failed to show any differences in efficacy between disulfiram and the placebo concerning the risk of alcohol consumption relapse and the number of alcohol abstinence days. The efficacy of disulfiram is based on the antabuse effect when combined with alcohol consumption. The patient is aware of the product's coercive effect, this is the basis of its efficacy. It is thus difficult to establish the product's efficacy versus placebo in a randomised double-blind study.
  The SPC of disulfiram has been amended to take into consideration several adverse effects that may be severe, in particular convulsions, encephalopathy and hepatitis. The many adverse effects associated with the antabuse effect of disulfiram are mentioned: neurological accidents, tachycardia, myocardial infarction, arrhythmia and respiratory depression.

Benefit of the medicinal product

- The actual clinical benefit* of AOTAL, ESPERAL and REVIA remains substantial.
- Approved for continuing non-hospital pharmacy reimbursement or for hospital treatment.

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This document was drafted on the basis of the Transparency Committee opinion dated 17 October 2018 (CT-15173, CT-16140, CT-16128) available at **www.has-sante.fr**

* The actual clinical benefit (ACB) of a medicinal product consists of its benefit particularly on the basis of its clinical performances and the severity of the disease treated. The HAS Transparency Committee assesses the ACB, which may besubstantial, moderate, low, or insufficient for the medicinal product to be covered by public funding.