# UNIT DOSES FOR IMMEDIATE RELEASE OF GHB OR OF ONE OF THE THERAPEUTICALLY ACCEPTABLE SALTS THEREOF, ADMINISTERED ORALLY, AND THE USE THEREOF TO MAINTAIN ALCOHOL ABSTINENCE

The present invention concerns immediate release, unit doses of GHB or one of the therapeutically acceptable salts thereof administered via oral route, and the use thereof for maintaining abstinence from alcohol.

**Summary**

In one aspect, there is provided a unit dose of GHB or one of the therapeutically acceptable salts thereof, sodium oxybate in particular, intended for the maintaining of alcohol abstinence in patients suffering from alcoholism, characterized in that the *in vitro* release of the active ingredient is higher than 85 % in fifteen minutes, and preferably 90 % in fifteen minutes, said unit dose being between 0.37 and 1.75 g.

In another aspect, there is provided a use of the unit dose of GHB or one of the therapeutically acceptable salts thereof as described herein in the manufacture of a medicament for obtaining alcohol abstinence in a patient, characterized in that three unit doses as described herein are to be taken daily to obtain alcohol abstinence of a patient.

**Detailed Description**

Sodium oxybate, which is the most widely used salt of hydroxybutyric acid (GHB), is employed for therapeutic purposes in the treatment of the following pathologies:

- alcohol dependence: treatment of alcohol withdrawal syndrome and maintaining of alcohol abstinence in alcohol-dependent patients;
- narcolepsy in patients suffering from cataplexy,
- anaesthesia.

It is listed by the 1971 convention on psychotropic substances.

For therapeutic use, it is important that the optimal dosage of sodium oxybate should be well determined to enhance the benefit-risk ratio and to avoid any risk of over- or under-dosage.

The treatment of alcohol dependence takes place in two phases.

During the first phase, the patients are weaned and optionally treated in the event of severe withdrawal syndrome. Alcohol withdrawal syndrome is commonly used to describe the group of symptoms which occur on gradual or sudden stopping of alcohol intake by alcohol-dependent patients. These symptoms translate as mental, behavioural and physical side effects. In the majority of cases the syndrome resolves spontaneously or under two- to

five-day treatment but mortality is not zero (Société Française d'Alcoologie, 2006). It is treated with anticonvulsants, antipsychotics or with sodium oxybate.

After weaning, a maintained abstinence phase is necessary to improve the patient's state of health and avoid the onset of pathologies related to alcoholism. Abstinence appears to be the only efficient method to halt or reduce the psychological disorders of alcoholism. It is also the only means to reduce impacts on physical health since it has been shown in numerous publications that the risks of alcohol-related morbidity and mortality occurrence are a function of the level of the daily consumption of alcohol.

Treatment of maintained abstinence is composed of psychosocial follow-up and pharmacological treatments over periods of several months.

10. The unit dose according to claim 9, characterized in that said oral form has a TMax lower than 40 minutes, and preferably lower than 30 minutes.

11. The unit dose according to one of claims 9 or 10, characterized in that said solid oral form is composed of granules.

12. The unit dose according to claim 11, characterized in that said granules are packaged in sachets, particularly in sticks.

13. The unit dose of GHB or one of the therapeutically acceptable salts thereof according to one of claims 11 or 12, characterized in that said granules have the following composition (given relative to the weight of the granules):

- active ingredient: 50 to 60 %;
- effervescent agent: 5 to 15 %;
- diluent: 2 to 18 %;
- binder: 3 to 10 %;
- substrate (solid core of the granule): 15 to 25 %;
- coating agent/ flavouring agent / sweetening agent / lubricant: 3 to 6 %.

14. The unit dose according to claim 13, characterized in that said granules have the following composition (given relative to the weight of the granules):

- Sodium oxybate (active ingredient): 56.02 %;
- Sodium bicarbonate (effervescent agent): 8.40 %;
- Magnesium aluminosilicate (diluent): 5.04 %;
- Povidone (binder): 5.60 %;
- Sugar spheres (substrate): 19.66 % (in a proportion of 62.5 % to 91.5 % sucrose per 8.5 % to 37.5 % starch);
- Coating agent: 0.95 % hypromellose, 0.10 % stearic acid, 0.05 % flavouring agent, 0.83 % sucralose (sweetening agent) and 3.34 % talc.

15. Use of the unit dose of GHB or one of the therapeutically acceptable salts thereof according to any of claims 1 to 14 in the manufacture of a medicament for obtaining alcohol abstinence in a patient, characterized in that three unit doses according to any of claims 1 to 14 are to be taken daily to obtain alcohol abstinence of a patient.