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 use of a unit dose of GHB or a therapeutically acceptable salt thereof as an active ingredient in the manufacture of a medicament for maintaining alcohol abstinence in a patient affected by alcoholism

wherein three unit doses of said GHB or a therapeutically acceptable salt thereof are to be taken daily, each of the unit doses comprising between 0.37 and 1.75 g of the active ingredient,

and the active ingredient has an *in vitro* release higher than 85 % in fifteen minutes in a medium at pH 1 (0.1 HCL),

and wherein the dosage of active ingredient for said patient is based on the daily alcohol consumption of the patient, independently of patient weight.

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.

CLAIMS

1. Use of a unit dose of GHB or a therapeutically acceptable salt thereof as an active ingredient in the manufacture of a medicament for maintaining alcohol abstinence in a patient affected by alcoholism

wherein three unit doses of said GHB or a therapeutically acceptable salt thereof are to be taken daily, each of the unit doses comprising between 0.37 and 1.75 g of the active ingredient,

and the active ingredient has an *in vitro* release higher than 85 % in fifteen minutes in a medium at pH 1 (0.1 HCL),

and wherein the dosage of active ingredient for said patient is based on the daily alcohol consumption of the patient, independently of patient weight.

2. The use according to claim 1, wherein each of the unit doses comprises between 0.75 and 1.25 g of the active ingredient.

3. The use according to claim 2, wherein each of the unit doses contains 0.75 g of the active ingredient.

4. The use according to claim 1, wherein each of the unit doses comprises between 0.37 and 0.62 g of the active ingredient.

5. The use according to claim 4, wherein each of the unit doses contains 0.37 g of the active ingredient.

6. The use according to claim 1, wherein each of the unit doses comprises between 1.25 and 1.75 g of the active ingredient.

7. The use according to claim 6, wherein each of the unit doses contains 1.50 g of the active ingredient.

8. The use according to claim 1, wherein each of the unit doses comprises between 0.62 and 0.87 g of the active ingredient.

9. The use according to claim 8, wherein each of the unit doses contains 0.75 g of the active ingredient.

10. The use according to any one of the previous claims, wherein the unit doses is in solid, semi-solid, semi-liquid or liquid oral form, these different forms having the same pharmacokinetic profile.

11. The use according to claim 10, wherein said solid oral form is composed of granules.

12. The use according to claim 11, wherein said granules are packaged in sachets.

13. The use according to claim 11, wherein said granules have the following composition (given relative to the weight of the granules):
active ingredient: 50 to 60% ;
effervescent agent: 5 to 15% ;
diluant: 2 to 18% ;
binder: 3 to 10% ;
substrate (solid core of the granules): 15 to 25% ;
coating agent / flavouring agent / sweetening agent / lubricant: 3 to 6%.

14. The use according to claim 13, wherein 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 (diluant): 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) et 3.34% talc.

15. The use according to claim 2 or 3, wherein the patient when said patient has mild or moderate alcohol dependence without liver disease.

16. The use according to claim 4 or 5, in a patient when said patient has mild or moderate alcohol dependence with liver disease.

17. The use according to claim 6 or 7, in a patient when said patient has severe or very severe alcohol dependence without liver disease.

18. The use according to claim 8 or 9, in a patient when said patient has severe or very severe alcohol dependence with liver disease.