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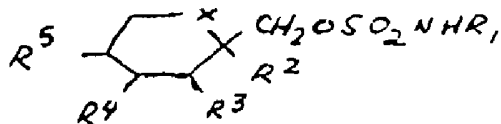
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(54) DERIVES ANTI-CONVULSIFS UTILES POUR TRAITER LA BOULIMIE NERVEUSE

(54) ANTICONVULSANT DERIVATIVES USEFUL IN TREATING BULIMIA NERVOSA

(57)

Anticonvulsant derivatives of formula: (I),  
wherein x is CH<sub>2</sub> or oxygen, for treating bulimia  
nervosa are disclosed.



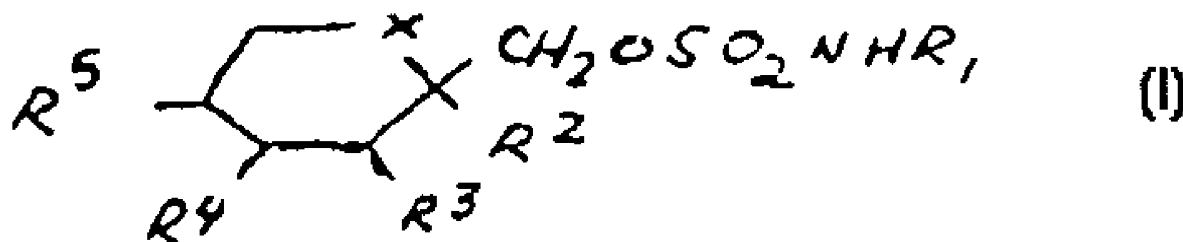
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(54) Titre : DERIVES ANTI-CONVULSIFS UTILES POUR TRAITER LA BOULIMIE NERVEUSE  
(54) Title: ANTICONVULSANT DERIVATIVES USEFUL IN TREATING BULIMIA NERVOSA



(57) Abrégé/Abstract:

Anticonvulsant derivatives of formula: (I), wherein x is CH<sub>2</sub> or oxygen, for treating bulimia nervosa are disclosed.





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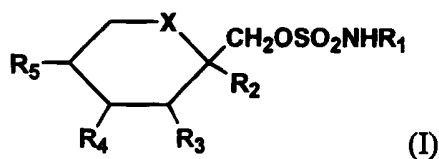
## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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<b>(21) International Application Number:</b> PCT/US00/02334 <b>(22) International Filing Date:</b> 31 January 2000 (31.01.00)  <b>(30) Priority Data:</b> 60/118,057      1 February 1999 (01.02.99)      US  <b>(71) Applicant:</b> ORTHO-MCNEIL PHARMACEUTICAL, INC. [US/US]; U.S. Route 202, Raritan, NJ 08869-0602 (US).  <b>(72) Inventor:</b> HOOPES, Scott, P.; 2335 Aldercrest, Eagle, ID 83616 (US).  <b>(74) Agents:</b> CIAMPORCERO, Audley, A., Jr. et al.; John- son & Johnson, One Johnson Plaza, New Brunswick, NJ 08903-7003 (US).		<b>(81) Designated States:</b> AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).  <b>Published</b> <i>With international search report.</i> <i>Before the expiration of the time limit for amending the</i> <i>claims and to be republished in the event of the receipt of</i> <i>amendments.</i>
<b>(54) Title:</b> USE OF ANTICONVULSANT DERIVATIVES FOR TREATING BULIMIA NERVOSA  <div style="text-align: center;"> </div> <b>(57) Abstract</b> Anticonvulsant derivatives of formula: (I), wherein x is CH <sub>2</sub> or oxygen, for treating bulimia nervosa are disclosed.		

# ANTICONVULSANT DERIVATIVES USEFUL IN TREATING BULIMIA NERVOSA

## BACKGROUND OF THE INVENTION

Compounds of Formula (I):



are structurally novel antiepileptic compounds that are highly effective anticonvulsants in animal tests (Maryanoff, B.E, Nortey, S.O., Gardlocki, J.F., Shank, R.P. and Dodgson, S.P. *J. Med. Chem.* 30, 880-887, 1987; Maryanoff, B.E., Costanzo, M.J., Shank, R.P., Schupsky, J.J., Ortegon, M.E., and Vaught J.L. *Bioorganic & Medicinal Chemistry Letters* 3, 2653-2656, 1993). These compounds are covered by US Patent No. 4,513,006. One of these compounds 2,3:4,5-bis-O-(1-methylethylidene)- $\beta$ -D-fructopyranose sulfamate known as topiramate has been demonstrated in clinical trials of human epilepsy to be effective as adjunctive therapy or as monotherapy in treating simple and complex partial seizures and secondarily generalized seizures (E. FAUGHT, B.J. WILDER, R.E. RAMSEY, R.A. REIFE, L D. KRAMER, G.W. PLEDGER, R.M. KARIM et. al., *Epilepsia* 36 (S4) 33, 1995; S.K. SACHDEO, R.C. SACHDEO, R.A. REIFE, P. LIM and G. PLEDGER, *Epilepsia* 36 (S4) 33, 1995), and is currently marketed for the treatment of simple and complex partial seizure epilepsy with or without secondary generalized seizures in approximately twenty countries including the United States, and applications for regulatory approval are presently pending in several additional countries throughout the world.

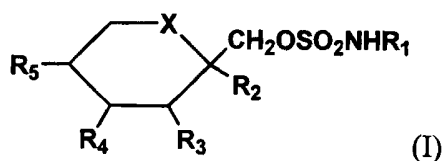
Compounds of Formula (I) were initially found to possess anticonvulsant activity in the

traditional maximal electroshock seizure (MES) test in mice (SHANK, R.P., GARDOCKI, J.F., VAUGHT, J.L., DAVIS, C.B., SCHUPSKY, J.J., RAFFA, R.B., DODGSON, S.J., NORTEY, S.O., and MARYANOFF, B.E., *Epilepsia* 35 450-460, 1994). Subsequent studies revealed that Compounds of Formula (I) were also highly effective in the MES test in rats. More recently topiramate was found to effectively block seizures in several rodent models of epilepsy (J. NAKAMURA, S. TAMURA, T. KANDA, A. ISHII, K. ISHIHARA, T. SERIKAWA, J. YAMADA, and M. SASA, *Eur. J. Pharmacol.* 254 83-89, 1994), and in an animal model of kindled epilepsy (A. WAUQUIER and S. ZHOU, *Epilepsy Res.* 24, 73-77, 1996).

Bulimia nervosa is characterized by recurrent episodes of binge eating associated with inappropriate compensatory behavior to prevent weight gain (Diagnostic Statistical Manual of the American Psychiatric Association IVth Edition). It is more common in females than males; self evaluation is unduly influenced by body shape and weight and occurs in persons with high rates of mood and impulse control disorders.

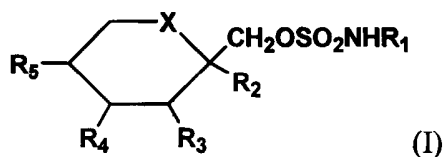
## DISCLOSURE OF THE INVENTION

Accordingly, it has been found that compounds of the following Formula (I):



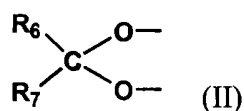
wherein X is O or CH<sub>2</sub>, and R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> and R<sub>5</sub> are as defined hereinafter are useful in treating bulimia.

More particularly, the present invention discloses the use of compounds of Formula (I):



wherein

- X is oxygen; R<sub>1</sub> is hydrogen or C<sub>1</sub>-C<sub>4</sub> alkyl, where alkyl includes straight and branched chain alkyl; and R<sub>2</sub> and R<sub>3</sub>, and R<sub>4</sub> and R<sub>5</sub>, together are a methylenedioxy group  
 5 of the following Formula (II):

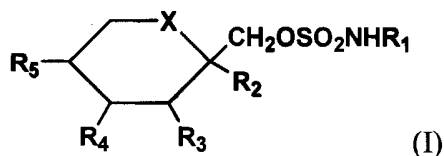


wherein

- R<sub>6</sub> and R<sub>7</sub> are the same or different and are hydrogen, C<sub>1</sub>-C<sub>3</sub> alkyl, where alkyl includes straight and branched chain alkyl, or are alkyl and are joined to form a  
 10 cyclopentyl or cyclohexyl ring, in the treatment of bulimia.

## DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

The sulfamates of the Invention are of the following Formula (I):

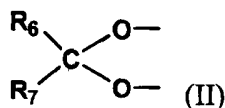


wherein

X is CH<sub>2</sub> or oxygen;

R<sub>1</sub> is hydrogen or C<sub>1</sub>-C<sub>4</sub> alkyl; and

- R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> and R<sub>5</sub> are independently hydrogen or C<sub>1</sub>-C<sub>3</sub> alkyl, and when X is CH<sub>2</sub>,  
 5 R<sub>4</sub> and R<sub>5</sub> may be alkene groups joined to form a benzene ring, and when X is oxygen, R<sub>2</sub>  
 and R<sub>3</sub> and/or R<sub>4</sub> and R<sub>5</sub> together may be a methylenedioxy group of the following  
 Formula (II):



wherein

- 10 R<sub>6</sub> and R<sub>7</sub> are the same or different and are hydrogen, C<sub>1</sub>-C<sub>3</sub> alkyl or are alkyl and  
 are joined to form a cyclopentyl or cyclohexyl ring.

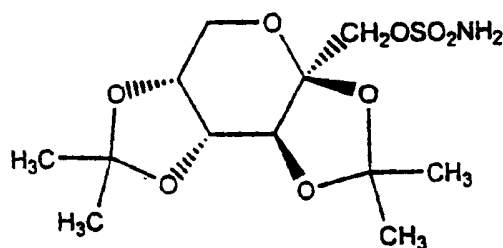
- R<sub>1</sub> in particular is hydrogen or alkyl of about 1 to 4 carbons, such as methyl, ethyl  
 iso-propyl, *n*-propyl, *n*-butyl, isobutyl, *sec*-butyl and *t*-butyl. Alkyl throughout this  
 specification includes straight and branched chain alkyl. Alkyl groups for R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub>,  
 15 R<sub>6</sub> and R<sub>7</sub> are of about 1 to 3 carbons and include methyl, ethyl, iso-propyl and *n*-propyl.  
 When X is CH<sub>2</sub>, R<sub>4</sub> and R<sub>5</sub> may combine to form a benzene ring fused to the 6-membered  
 X-containing ring, i.e., R<sub>4</sub> and R<sub>5</sub> are defined by the alkatrienyl group =C-CH=CH-CH=.

- A particular group of compounds of Formula (I) is that wherein X is oxygen and  
 both R<sub>2</sub> and R<sub>3</sub>, and R<sub>4</sub> and R<sub>5</sub> together are methylenedioxy groups of the Formula (II),  
 20 wherein R<sub>6</sub> and R<sub>7</sub> are both hydrogen, both alkyl, or combine to form a spiro cyclopentyl  
 or cyclohexyl ring, in particular where R<sub>6</sub> and R<sub>7</sub> are both alkyl such as methyl. A second  
 group of compounds is that wherein X is CH<sub>2</sub> and R<sub>4</sub> and R<sub>5</sub> are joined to form a benzene  
 ring. A third group of compounds of Formula (I) is that wherein both R<sub>2</sub> and R<sub>3</sub> are  
 hydrogen.

A particularly preferred embodiment of the present invention is a group of compounds of Formula (I) wherein X is oxygen, R<sub>1</sub> is hydrogen or C<sub>1</sub>-C<sub>4</sub> alkyl, and R<sub>2</sub> and R<sub>3</sub>, and R<sub>4</sub> and R<sub>5</sub>, together are a methylenedioxy group of Formula (II), wherein R<sub>6</sub> and R<sub>7</sub> are the same or different and are hydrogen, C<sub>1</sub>-C<sub>3</sub> alkyl, or are alkyl and are joined  
5 to form a cyclopentyl or cyclohexyl ring.

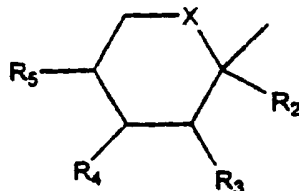
A particularly preferred compound for use in the methods of the present invention is 2,3:4,5-bis-O-(1-methylethylidene)- $\beta$ -D-fructopyranose sulfamate, known as topiramate. Topiramate has the following structural formula:





The compounds of formula (I) may be synthesized by the following methods:

- (a) Reaction of an alcohol of the formula  $RCH_2OH$  with a chlorosulfamate of the formula  $ClSO_2NH_2$  or  $ClSO_2NHR_1$  in the presence of a base such as potassium *n*-butoxide or sodium hydride at a temperature of about  $-20^\circ$  to  $25^\circ$  C and in a solvent such as toluene, THF or dimethylformamide wherein R is a moiety of the following formula (III):



- (b) Reaction of an alcohol of the formula  $RCH_2OH$  with sulfurylchloride of the formula  $SO_2Cl_2$  in the presence of a base such as triethylamine or pyridine at a temperature of about  $-40^\circ$  to  $25^\circ$  C in a solvent such as diethyl ether or methylene chloride to produce a chlorosulfate of the formula  $RCH_2OSO_2Cl$ .

The chlorosulfate of the formula  $RCH_2OSO_2Cl$  may then be reacted with an amine of the formula  $R_1NH_2$  at a temperature of about  $-40^\circ$  to  $25^\circ$  C in a solvent such as methylene chloride or acetonitrile to produce a compound of formula (I). The reaction conditions for (b) are also described by T. Tsuchiya et al. in Tet. Letters, No. 36, p. 3365 to 3368 (1978).

- (c) Reaction of the chlorosulfate  $RCH_2OSO_2Cl$  with a metal azide such as sodium azide in a solvent such as methylene chloride or acetonitrile yields an azidosulfate of the formula  $RCH_2OSO_2N_3$  as described by M. Hedayatullah in Tet. Lett. p. 2455-2458 (1975). The azidosulfate is then reduced to a compound of formula (I) wherein  $R_1$  is hydrogen by catalytic hydrogenation, e.g. with a noble metal and  $H_2$  or by heating with copper metal in a solvent such as methanol.

The starting materials of the formula  $RCH_2OH$  may be obtained commercially or as known in the art. For example, starting materials of the formula  $RCH_2OH$  wherein both  $R_2$  and  $R_3$  and  $R_4$  and  $R_5$  are identical and are of the formula (II) may be obtained by the method of R. F. Brady in Carbohydrate Research, Vol. 14, p. 35 to 40 (1970) or by reaction of the trimethylsilyl enol ether of a  $R_6COR_7$  ketone or aldehyde with fructose at a temperature of about 25° C, in a solvent such as a halocarbon, e.g. methylene chloride in the presence of a protic acid such as hydrochloric acid or a Lewis Acid such as zinc chloride. The trimethylsilyl enol ether reaction is described by G. L. Larson et al in J. Org. Chem. Vol. 38, No. 22, p. 3935 (1973).

Further, carboxylic acids and aldehydes of the formulae  $RCOOH$  and  $RCHO$  may be reduced to compounds of the formula  $RCH_2OH$  by standard reduction techniques, e.g. reaction with lithium aluminum hydride, sodium borohydride or borane-THF complex in an inert solvent such as diglyme, THF or toluene at a temperature of about 0° to 100° C, e.g. as described by H.O. House in "Modern Synthetic Reactions", 2<sup>nd</sup> Ed., pages 45 to 144 (1972).

The compounds of formula I may also be made by the known processes disclosed in U.S. Patent Nos. 4,513,006 and 5,387,700. More particularly, topiramate may be prepared following the process described in Examples 1 to 3 of U.S. 5,387,700.

The compounds of formula I include the various individual isomers as well as the racemates thereof, e.g., the various alpha and beta attachments, i.e., below and above the plane of the drawing, of  $R_2$ ,  $R_3$ ,  $R_4$  and  $R_5$  on the 6-membered ring. Preferably, the oxygens of the methylenedioxy group (II) are attached on the same side of the 6-membered ring.

The term "subject" as used herein, refers to an animal, preferably a mammal, most preferably a human, who has been the object of treatment, observation or experiment.

The term "therapeutically effective amount" as used herein, means that amount of active compound or pharmaceutical agent that elicits the biological or medicinal response in a tissue system, animal or human that is being sought by a researcher,

veterinarian, medical doctor or other clinician, which includes alleviation of the symptoms of the disease or disorder being treated.

It has been suggested that variations in brain GABA metabolism may be involved in the control of food intake in rats and that experimental brain GABA elevation produced anorexia in adult female rats (Coscina DV, *GABA and feeding: reversal of overeating by central GABA-transaminase inhibition*, Progress in Neuro-Psychopharmacology & Biological Psychiatry, 7(4-6):463-7,1983). It has also been shown that endogenous lateral hypothalamic glutamate acts to regulate natural eating and body weight in rats (Stanley BG, Willett VL 3<sup>rd</sup>, Donias HW, Dee MG 2<sup>nd</sup>, Duva MA, *Lateral hypothalamic NMDA receptors and glutamate as physiological mediators of eating and weight control*, American Journal of Physiology, 270(2Pt 2):R443-9, 1996 Feb.). Based on the known enhancement of brain GABA activity and reduced glutamate receptor activity of topiramate, we hypothesize that there is potential efficacy of topiramate in the treatment of bulimia.

For treating bulimia, a compound of formula (I) may be employed at a total daily dosage in the range of about 15 mg to about 500 mg, preferably, about 16 mg to about 200 mg, for an average adult human, administered one to four times per day, preferably, one to two times per day. A unit dose typically contains about 16 to about 300 mg, preferably, about 16 to about 200 mg, of the active ingredient.

Optimal dosages to be administered may be readily determined by those skilled in the art, and will vary with the particular compound used, the mode of administration, the strength of the preparation, the mode of administration, and the advancement of the disease condition. In addition, factors associated with the particular patient being treated, including patient age, weight, diet and time of administration, will result in the need to adjust dosages.

To prepare the pharmaceutical compositions of this invention, one or more sulfamate compounds of formula (I) are intimately admixed with a pharmaceutical carrier according to conventional pharmaceutical compounding techniques, which carrier may take a wide variety of forms depending on the form of preparation desired for

administration, e.g., oral, by suppository, or parenteral. In preparing the compositions in oral dosage form, any of the usual pharmaceutical media may be employed. Thus, for liquid oral preparations, such as for example, suspensions, elixirs and solutions, suitable carriers and additives include water, glycols, oils, alcohols, flavoring agents, preservatives, coloring agents and the like; for solid oral preparations such as, for example, powders, capsules and tablets, suitable carriers and additives include starches, sugars, diluents, granulating agents, lubricants, binders, disintegrating agents and the like. Because of their ease in administration, tablets and capsules represent the most advantageous oral dosage unit form, in which case solid pharmaceutical carriers are obviously employed. If desired, tablets may be sugar coated or enteric coated by standard techniques. Suppositories may be prepared, in which case cocoa butter could be used as the carrier. For parenterals, the carrier will usually comprise sterile water, though other ingredients, for example, for purposes such as aiding solubility or for preservation, may be included. Injectable solutions may also be prepared in which case appropriate stabilizing agents may be employed. Topiramate is currently available for oral administration in round tablets containing 25 mg, 100 mg or 200 mg of active agent. The tablets contain the following inactive ingredients: lactose hydrous, pregelatinized starch, microcrystalline cellulose, sodium starch glycolate, magnesium stearate, purified water, carnauba wax, hydroxypropyl methylcellulose, titanium dioxide, polyethylene glycol, synthetic iron oxide, and polysorbate 80.

The pharmaceutical compositions herein will contain, per dosage unit, e.g., tablet, capsule, powder injection, teaspoonful, suppository and the like from about 25 to about 200 mg of the active ingredient.

The following Examples are set forth to aid in the understanding of the invention, and are not intended and should not be construed to limit in any way the invention set forth in the claims which follow thereafter.

#### EXAMPLE 1

**Patient 01:** Patient started topiramate at a dose of 25 mg qhs and titrated by 25 mg/week to a dose of 100 mg/day. Within 1 month, patient had stopped bingeing for 2 weeks (had been bingeing daily) and felt control over her eating. After 5 months,

patient was still bingeing and purging less, but has parasthesia so the timing of her topiramate was adjusted to try and relieve this. She has not lost weight although not gained either in spite of increased activity. She had run out of topiramate 1 week prior to this appointment and her mood had sharply deteriorated. Wellbutrin was added at this visit. Three weeks later, patient was feeling well, continued benefit to her bulimia, and parasthesias have resolved with topiramate 100 mg qd dosing.

#### EXAMPLE 2

**Patient 02:** Patient started topiramate 25 mg qhs and titrated by 25 mg/week to dose of 100 mg/day. At first visit, she was purging 3 times/day to 3 times/week. After 3 weeks (topiramate 75 mg/hs), she is now satisfied when she eats small amounts of food and has not over-eaten or felt guilty or purges. After 3 months, patient has lost weight, is sleeping well and energetic. No adverse effects on 100 mg qhs.

#### EXAMPLE 3

**Patient 03:** Patient very depressed, thoughts of suicide for years, currently on topiramate and has been purging less than 1/day which is a decrease. At this visit, increased topiramate to 100 mg qhs (not sure what dose was before this) as seems to have decreased purging. Two weeks later, patient is more depressed, sedated and purging more; changing depression medicines now. Two days later, patient presents urgently as throwing up uncontrollably due to stress and apprehension. Patient also has migraines which cause emesis. Patient admitted to hospital for 4 days. After hospitalization, mood is improved. Topiramate increased to 175 mg/day (100 mg qhs and 25 mg tid 1 hour prior to meals). Two weeks later, her mood is much improved and purging only once every other day which is a marked decrease.

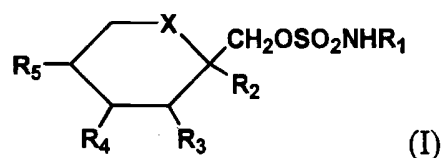
#### EXAMPLE 4

**Patient 04:** Patient depressed and purging 5/day – lots of family issues and lot of weight gain from current medicines - admitted to hospital for 2 weeks and taking topiramate 50 mg qhs. Topiramate was increased to 200 mg qhs while in hospital. Three weeks after hospitalization, patient is sleeping better, not purging and has lost 30 lbs. Two weeks later, patient continues doing well, sleeping well and happy about weight loss; no adverse effects. One month later, continues doing well, has not binged and has lost the 30 lbs about which she is very happy. She continues topiramate at 200 mg qhs.

While the foregoing specification teaches the principles of the present invention, with examples provided for the purpose of illustration, it will be understood that the practice of the invention encompasses all of the usual variations, adaptations and/or modifications as come within the scope of the following claims and their equivalents.

The embodiments of the invention in which an exclusive property or privilege is claimed are defined as follows:

1. The use of a compound of the Formula (I):

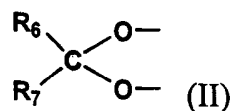


5 wherein

X is oxygen;

R<sub>1</sub> is hydrogen or C<sub>1</sub>-C<sub>4</sub> alkyl, where alkyl includes straight and branched chain alkyl; and

10 R<sub>2</sub> and R<sub>3</sub>, and R<sub>4</sub> and R<sub>5</sub>, together are a methylenedioxy group of the following Formula (II):

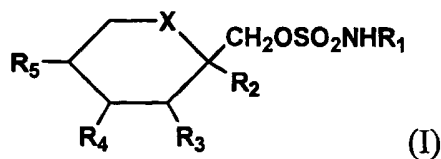


wherein

15 R<sub>6</sub> and R<sub>7</sub> are the same or different and are hydrogen, C<sub>1</sub>-C<sub>3</sub> alkyl, where alkyl includes straight and branched chain alkyl, or R<sub>6</sub> and R<sub>7</sub> together with the carbon atom to which they are attached form a cyclopentyl or cyclohexyl ring; in a therapeutically effective amount for treating bulimia nervosa in a subject in need thereof.

2. The use of claim 1, wherein the compound of Formula (I) is topiramate.
3. The use of claim 1 or 2, wherein the therapeutically effective amount is  
20 from about 15 mg to about 500 mg per day.

4. The use of claim 1 or 2, wherein the therapeutically effective amount is from about 16 mg to about 200 mg per day.
5. The use of claim 1 or 2, wherein the therapeutically effective amount is from about 16 mg to about 300 mg per unit dose.
- 5 6. The use of claim 1 or 2, wherein the therapeutically effective amount is from about 16 mg to about 200 mg per unit dose.
7. The use of claim 1 or 2, wherein the compound of Formula (I) is in admixture with a pharmaceutically acceptable carrier.
8. The use of a compound of the Formula (I):

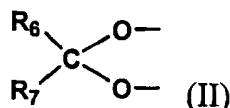


wherein

X is oxygen;

R<sub>1</sub> is hydrogen or C<sub>1</sub>-C<sub>4</sub> alkyl, where alkyl includes straight and branched chain alkyl; and

- 15 R<sub>2</sub> and R<sub>3</sub>, and R<sub>4</sub> and R<sub>5</sub>, together are a methylenedioxy group of the following Formula (II):



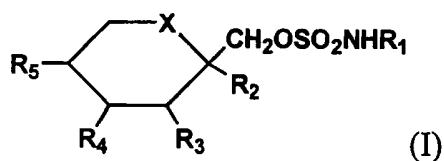
wherein

- 20 R<sub>6</sub> and R<sub>7</sub> are the same or different and are hydrogen, C<sub>1</sub>-C<sub>3</sub> alkyl, where alkyl includes straight and branched chain alkyl, or R<sub>6</sub> and R<sub>7</sub> together with the



carbon atom to which they are attached form a cyclopentyl or cyclohexyl ring; in a therapeutically effective amount for decreasing bingeing and purging episodes in a subject suffering from bulimia nervosa.

9. The use of claim 8, wherein the compound of Formula (I) is topiramate.
- 5 10. The use of claim 8 or 9, wherein the therapeutically effective amount is from about 15 mg to about 500 mg per day.
11. The use of claim 8 or 9, wherein the therapeutically effective amount is from about 16 mg to about 200 mg per day.
12. The use of claim 8 or 9, wherein the therapeutically effective amount is  
10 from about 16 mg to about 300 mg per unit dose.
13. The use of claim 8 or 9, wherein the therapeutically effective amount is from about 16 mg to about 200 mg per unit dose.
14. The use of claim 8 or 9, wherein the compound of Formula (I) is in admixture with a pharmaceutically acceptable carrier.
- 15 15. A pharmaceutical composition for treating bulimia nervosa in a patient which comprises as active ingredient a compound of Formula (I):

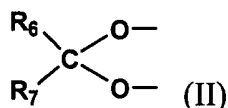


wherein

X is oxygen;

- 20  $R_1$  is hydrogen or  $C_1$ - $C_4$  alkyl, where alkyl includes straight and branched chain alkyl; and

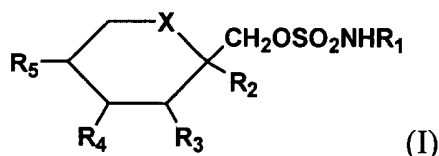
R<sub>2</sub> and R<sub>3</sub>, and R<sub>4</sub> and R<sub>5</sub>, together are a methylenedioxy group of the following Formula (II):



wherein

- 5        R<sub>6</sub> and R<sub>7</sub> are the same or different and are hydrogen, C<sub>1</sub>-C<sub>3</sub> alkyl, where alkyl includes straight and branched chain alkyl, or R<sub>6</sub> and R<sub>7</sub> together with the carbon atom to which they are attached form a cyclopentyl or cyclohexyl ring; together with a pharmaceutically acceptable carrier therefor.
16.    The pharmaceutical composition of claim 15, wherein the compound of
- 10    Formula (I) is topiramate.
17.    The pharmaceutical composition of claim 15 or 16, wherein the compound of Formula (I) is used in a therapeutically effective amount of from about 15 mg to about 500 mg per day.
18.    The pharmaceutical composition of claim 15 or 16, wherein the compound
- 15    of Formula (I) is used in a therapeutically effective amount of from about 16 mg to about 200 mg per day.
19.    The pharmaceutical composition of claim 15 or 16, wherein the compound of Formula (I) is used in a therapeutically effective amount of from about 16 mg to about 300 mg per unit dose.
- 20    20.    The pharmaceutical composition of claim 15 or 16, wherein the compound of Formula (I) is used in a therapeutically effective amount of from about 16 mg to about 200 mg per unit dose.

21. A pharmaceutical composition for decreasing bingeing and purging episodes in a subject suffering from bulimia nervosa, which comprises as active ingredient a compound of Formula (I):

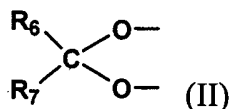


5 wherein

X is oxygen;

R<sub>1</sub> is hydrogen or C<sub>1</sub>-C<sub>4</sub> alkyl, where alkyl includes straight and branched chain alkyl; and

10 R<sub>2</sub> and R<sub>3</sub>, and R<sub>4</sub> and R<sub>5</sub>, together are a methylenedioxy group of the following Formula (II):



wherein

15 R<sub>6</sub> and R<sub>7</sub> are the same or different and are hydrogen, C<sub>1</sub>-C<sub>3</sub> alkyl, where alkyl includes straight and branched chain alkyl, or R<sub>6</sub> and R<sub>7</sub> together with the carbon atom to which they are attached form a cyclopentyl or cyclohexyl ring; together with a pharmaceutically acceptable carrier therefor.

22. The pharmaceutical composition of claim 21, wherein the compound of Formula (I) is topiramate.

20 23. The pharmaceutical composition of claim 21 or 22, wherein the compound of Formula (I) is used in a therapeutically effective amount of from about 15 mg to about 500 mg per day.

24. The pharmaceutical composition of claim 21 or 22, wherein the compound of Formula (I) is used in a therapeutically effective amount of from about 16 mg to about 200 mg per day.
25. The pharmaceutical composition of claim 21 or 22, wherein the compound  
5 of Formula (I) is used in a therapeutically effective amount of from about 16 mg to about 300 mg per unit dose.
26. The pharmaceutical composition of claim 21 or 22, wherein the compound of Formula (I) is used in a therapeutically effective amount of from about 16 mg to about 200 mg per unit dose.