

FORM 1

623731

REGULATION 9

COMMONWEALTH OF AUSTRALIA

PATENTS ACT 1952

APPLICATION FOR A STANDARD PATENT

We, WARNER-LAMBERT COMPANY, a Corporation organised under the laws of the State of Delaware, United States of America, of 2800 Plymouth Road, Ann Arbor, Michigan 48105, United States of America, hereby apply for the grant of a Standard Patent for an invention

entitled:-

"WATER DISPERSIBLE GEMFIBROZIL COMPOSITIONS"

which is described in the accompanying Complete Specification.

Details of basic application:-

Number: 07/305,081

Country: United States of America

Date: 2nd February, 1989

Our address for service is:

SHELSTON WATERS

55 Clarence Street

SYDNEY, N.S.W. 2000.

DATED this 1st Day of February, 1990

WARNER-LAMBERT COMPANY

By 
Fellow Institute of Patent Attorneys of Australia
of SHELSTON WATERS

To: The Commissioner of Patents
WODEN A.C.T. 2606

File: D.B. W-120

Fee: \$150.00

5012810 01/02/90

CONVENTION APPLICATION BY A COMPANY

FORM 8 - REGULATION 12 (2)

AUSTRALIA
PATENTS ACT 1952

DECLARATION IN SUPPORT OF A CONVENTION APPLICATION FOR A PATENT

In support of the Convention Application made by.....

(a) Here Insert (In full) Name of Company. (a) WARNER-LAMBERT COMPANY

(hereinafter referred to as "Applicant") for a patent for an invention entitled:

(b) Here Insert Title of Invention. (b) "WATER DISPERSIBLE GEMFIBROZIL COMPOSITIONS"

(c) and (d) Here Insert Full Name and Address of Company Official authorised to make declaration.

(c) Christine Alice Trautwein, Assistant Secretary
of (d) 2800 Plymouth Road, Ann Arbor, Michigan 48105 USA

do solemnly and sincerely declare as follows:

1. I am authorised by Applicant to make this declaration on its behalf.

2. The basic Application(s) as defined by section 141 of the Act was / were made

(e) Here Insert Basic Country followed by date of Basic Application.

In (e) the U.S.A. on the 2nd day of February 1989 19

(f) Here Insert Full Name(s) of Applicant(s) in Basic Country.

by (f) Isaac Ghebrey-Sellassie, Uma Iyer, Robert Harry Gordon, Mahdi Bakir Fawzi

In on the day of 19

by

in on the day of 19

by

in on the day of 19

by

(g) Here Insert (In full) Name and Address of actual inventor or inventors.

3. (g) ISAAC GHEBRE-SELLASSIE, 359 Dell Place, Stanhope, New Jersey 07874; ROBERT HARRY GORDON, 134 Lincoln Avenue, Dover, New Jersey 07801; UMA IYER, 7 Florie Farm Road, Mendham, New Jersey 07945; MAHDI BAKIR FAWZI, 11 Timberline Drive, Flanders, New Jersey 07836, all of United States of America. is/are

the actual inventor(s) of the invention and the facts upon which Applicant is entitled to make the Application are as follows:

The applicant is the assignee of the actual inventors.

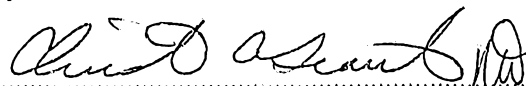
See reverse side of this form for guidance in completing this part.

4. The basic Application(s) referred to in paragraph 2 of this Declaration was/were the first Application(s) made in a Convention country in respect of the invention, the subject of the Application.

DECLARED at Ann Arbor, Michigan U.S.A.

this 8th day of December 1989

(h) Personal Signature of Declarant (c) (no seal, witness or legalisation).

(h) 
(Signature of Declarant)

(12) PATENT ABRIDGMENT (11) Document No. AU-B-48993/90
(19) AUSTRALIAN PATENT OFFICE (10) Acceptance No. 623731

- (54) Title
WATER DISPERSIBLE GEMFIBROZIL COMPOSITIONS
- International Patent Classification(s)
(51)⁵ A61K 031/19 A61K 009/10
- (21) Application No. : 48993/90 (22) Application Date : 01.02.90
- (30) Priority Data
- (31) Number (32) Date (33) Country
305081 02.02.89 US UNITED STATES OF AMERICA
- (43) Publication Date : 09.08.90
- (44) Publication Date of Accepted Application : 21.05.92
- (71) Applicant(s)
WARNER-LAMBERT COMPANY
- (72) Inventor(s)
ISAAC GHEBRE-SELLASSIE; ROBERT HARRY GORDON; UMA IYER; MAHDI BAKIR FAWZI
- (74) Attorney or Agent
SHELSTON WATERS, 55 Clarence Street, SYDNEY NSW 2000
- (56) Prior Art Documents
US 4132753
- (57) Claim

1. A water-dispersible formulation of gemfibrozil comprising finely divided particles of pure gemfibrozil uniformly coated with a mixture of a wax and at least one hydrophilic material selected from the group consisting of fatty acid alcohols, fatty acid esters, polyols, cellulose derivatives, and vinyl derivatives, the ratio of wax to hydrophilic material being from about 1:0.1 to about 0.1:1 said coated particles in turn being overcoated with a minor amount of a surfactant.

5. A water-dispersible formulation of gemfibrozil according to claim 1 wherein a first portion of the finely divided particles of pure gemfibrozil uniformly coated with a mixture of a wax and stearyl alcohol to provide relatively immediate release and a second portion of the finely divided particles of pure gemfibrozil uniformly coated with a mixture of a wax and hydrogenated castor oil to provide relatively sustained release.

623731

COMMONWEALTH OF AUSTRALIA

FORM 10

PATENTS ACT 1952

C O M P L E T E S P E C I F I C A T I O N

FOR OFFICE USE:

	Class	Int.Class
Application Number:		
Lodged:		

Complete Specification Lodged:
Accepted:
Published:

Priority:

Related Art:

.....

Name of Applicant: WARNER-LAMBERT COMPANY

.....

Address of Applicant: 2800 Plymouth Road, Ann Arbor, Michigan
48105, United States of America

Actual Inventor: Isaac Ghebre-Sellassie, Robert Harry
Gordon, Uma Iyer and Mahdi Bakir Fawzi

.....

Address for Service: SHELSTON WATERS, 55 Clarence Street, Sydney

Complete Specification for the Invention entitled:

.....

"WATER DISPENSIBLE GEMFIBROZIL COMPOSITIONS"

The following statement is a full description of this invention,
including the best method of performing it known to us:-

WATER DISPERSIBLE GEMFIBROZIL COMPOSITIONS

5 The present invention relates to a water-dispersible formulation of gemfibrozil.

Background

10 Gemfibrozil, or 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoic acid, is a widely used antihyperlipoproteinemic agent which, because of the required large dose, generally is administered several times a day in the form of multiple capsules. Although it would be desirable to administer the agent in a water-dispersible formulation, this approach heretofore has been unattainable because of the unpleasant burning after-taste which it produces in the buccal mucosa.

15 It also would be beneficial to provide such water-dispersible formulations with sustained release properties so as to reduce the number of times the drug must be administered.

20 British Application 2,179,254 discloses compositions of analgesic propionic acid derivatives (such as ibuprofen) coated with a methacrylic-acrylic acid copolymer, then with a methacrylic ester copolymer, and finally with a mixture of polysorbate 80 and
25 hydroxypropyl methylcellulose.

EPO-A 8600802 discloses sustained release compositions of polyethylene glycol and an amphiphilic compound.

5 French Application 2,554,717 discloses sustained release compositions which employs as the matrix a vinylpyrrolidone-vinyl acetate copolymer and an acrylic polymer cross-linked with polyallyl sucrose. (See also Belgian application 901007.)

10 U.S. Patent No. 4,132,753 discloses controlled release granules in which the powdered medicament is heated so as to sink into a finely divided wax material.

15 U.S. Patent No. 4,195,084 discloses a liquid suspension of finely ground tall oil sitosterols for use in reducing hypercholesteremia.

U.S. Patent No. 4,263,272 discloses three component formulations of bile acids which release gradually or in two stages.

20 U.S. Patent No. 4,291,016 discloses pharmaceutical compositions having a matrix core coated with hydroxypropyl methyl cellulose.

25 U.S. Patent No. 4,533,562 discloses tablets coated with a film-forming polymer such as hydroxypropyl methylcellulose and a liquid plasticizer such as polyethylene glycol.

U.S. Patent No. 4,661,162 discloses an enteric soluble composition containing a mixture of an entericsoluble polymer such as (m)ethyl acrylate/methacrylate copolymers and a polyanionic
5 polymer such as alginic acid and its salts.

Detailed Description

The present invention provides a water-dispersible formulation of gemfibrozil which can provide either immediate release, sustained release, or a combination of
10 immediate and sustained release. In particular, this invention employs a formulation in which finely divided particles of pure gemfibrozil are uniformly coated with a mixture of a wax and at least one hydrophilic material and the coated particles in turn are overcoated with a
15 minor amount of a surfactant, optionally together with flavoring agents.

The wax component is typically a conventional pharmaceutically acceptable microcrystalline wax. The hydrophilic materials are generally pharmaceutically
20 acceptable compounds of the alcohol and ester type such as fatty acid alcohols, fatty acid esters, polyols, cellulose derivatives, and vinyl derivatives. A preferred hydrophilic material is stearyl alcohol.

The ratio of wax to hydrophilic material is from
25 about 1:0.1 to about 0.1:1. A preferred range is from about 1:1 to about 5:1 of hydrophilic material:wax.

A coating formulation is prepared by mixing the wax and the hydrophilic material, optionally in the presence



of a small amount of a plasticizer such as polyethylene glycol. Finely divided particles of pure gemfibrozil then are uniformly coated with this mixture.

5 The apparatus employed to treat substrates with the instant coating materials is not critical. Generally, any device will suffice as long as it can effectively coat the medicament or other ingestible agent with a sufficient quantity of the coating to hide the bad taste of the gemfibrozil. One preferred type of coating device
10 is a fluid bed apparatus.

Following coating, the coated particles are in turn overcoated with a small amount, preferably 2-3 weight percent of a pharmaceutically acceptable surfactant, as for example sodium lauryl sulfate or polysorbate 80
15 dissolved in a aqueous carrier. This surfactant overcoat can be admixed with suitable flavoring agents which provide a pleasant taste but do not affect the operation of the formulation. The overcoat formulation can be simply sprayed on the coated particles and the excess
20 water then removed.

The resulting formulation has the appearance of a powder and is palatable and readily dispersible in ordinary water for oral administration. The coating composition has solubility characteristics which make it
25 practically insoluble in the mouth, but readily disintegrates in the acid environment provided by the gastric juices of the stomach. -----



In a further embodiment, the formulation includes a first portion of finely divided particles of pure gemfibrozil uniformly coated with a mixture of a wax and hydrophilic material such as stearyl alcohol (to provide relatively immediate release as described above) and a second portion of the finely divided particles of pure gemfibrozil uniformly coated with a mixture of a wax and a hydrophobic material to provide relatively sustained release. A preferred hydrophobic material is hydrogenated castor oil.

The following examples will serve to further typify the nature of the invention but should not be construed as being a limitation on the scope thereof, which scope is defined solely by the appended claims.

EXAMPLE 1

A coating formulation is prepared from the following components:

<u>Ingredient</u>	<u>Parts by weight</u>
-------------------	------------------------

Stearyl alcohol	3 parts
-----------------------	---------

Microcrystalline wax	1 part
----------------------------	--------

Polyethylene glycol 400	0.16 part
-------------------------------	-----------

Finely divided gemfibrozil particles are uniformly coated with the above formulation and then sprayed with an overcoat formulation of the following composition:

Sodium lauryl sulfate	3 parts
-----------------------------	---------

Purified water	97 parts
----------------------	----------

The overcoated particles are dried and packaged.

EXAMPLE 2

A sustained release coating formulation is prepared from the following components:

<u>Ingredient</u>	<u>Parts by weight</u>
-------------------	------------------------

5	Hydrogenated castor oil 3 parts
	Microcrystalline wax 1 part
	Polyethylene glycol 400 0.08 part

Finely divided gemfibrozil particles are uniformly coated with the above formulation and then sprayed with an overcoat formulation of the following composition:

10	Sodium lauryl sulfate 3 parts
	Purified water 97 parts

The overcoated particles are dried and then mixed with an equal amount by weight of coated particles prepared in accordance with Example 1.

15

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:-

1. A water-dispersible formulation of gemfibrozil comprising finely divided particles of pure gemfibrozil uniformly coated with a mixture of a wax and at least one hydrophilic material selected from the group consisting
5 of fatty acid alcohols, fatty acid esters, polyols, cellulose derivatives, and vinyl derivatives, the ratio of wax to hydrophilic material being from about 1:0.1 to about 0.1:1 said coated particles in turn being overcoated with a minor amount of a surfactant.
2. A water-dispersible formulation of claim 1 wherein the wax is a microcrystalline wax.
3. A water-dispersible formulation of gemfibrozil according to claim 1 or 2 wherein the hydrophilic material is stearyl alcohol.
4. A water-dispersible formulation of gemfibrozil according to any one of claims 1 to 3 wherein the surfactant is sodium lauryl sulfate.
5. A water-dispersible formulation of gemfibrozil according to claim 1 wherein a first portion of the finely divided particles of pure gemfibrozil uniformly coated with a mixture of a wax and stearyl alcohol to
5 provide relatively immediate release and a second portion of the finely divided particles of pure gemfibrozil uniformly coated with a mixture of -----



a wax and hydrogenated castor oil to provide relatively sustained release.

6. A water-dispensible formulation of gemfibrozil substantially as herein described with reference to any one of the examples.

DATED this 1st Day of February, 1990

WARNER-LAMBERT COMPANY

Attorney: IAN ERNST
Fellow Institute of Patent Attorneys of Australia
of SHELSTON WATERS