SG 9705772-3
RTMP'S COPY

PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 :
C07D 215/56, 471/04, A61K 31/435 // (C07D 471/04, 221:00, 221:00)

A1

(11) International Publication Number: WO 96/37475

(43) International Publication Date: 28 November 1996 (28.11.96)

(21) International Application Number: PCT/US96/05899

(22) International Filing Date: 26 April 1996 (26.04.96)

(30) Priority Data:
08/452,208 26 May 1995 (26.05.95) US

(71) Applicant: WARNER-LAMBERT COMPANY [US/US]; 201 Tabor Road, Morris Plains, NJ 07950 (US).

(72) Inventors: DOZEMAN, Gary, Jay; 1639 Lakeview Drive, Zeeland, MI 49464 (US). PORTER, Kenneth, Thomas; 14073 Deercove Drive, Holland, MI 49424 (US). WEMPLE, James, Norton; 14211 Deercove Drive, Holland, MI 49424 (US).

(74) Agents: RYAN, M., Andrea; Warner-Lambert Company, 201 Tabor Road, Morris Plains, NJ 07950 (US) et al.

(81) Designated States: AU, CA, CZ, EE, HU, JP, LT, LV, MX, NZ, PL, RO, SG, SI, SK, Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published
With international search report.

(54) Title: METHOD FOR MAKING QUINOLONE CARBOXYLIC ACIDS OR NAPHTHYRIDINE CARBOXYLIC ACIDS IN FREE BASE FORM

(57) Abstract

The present invention provides a method of making quinolone carboxylic acids or naphthyridine carboxylic acids in free base form, the method comprising dissolving a quinolone carboxylic acid salt or naphthyridine carboxylic acid salt in a solvent system to form a solution; combining the solution containing the quinolone carboxylic acid salt or naphthyridine carboxylic acid salt with a calcium salt in an amount in the range of about 0.01 % to about 5.0 % by weight of the quinolone carboxylic acid salt or naphthyridine carboxylic acid salt and a base, the combination resulting in the formation of a precipitate; and collecting the precipitate. Also provided is a solid bulk pharmaceutical chemical composition comprising 7-(3-amino-1-pyrrolidinyl)-8-chloro-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxoquinoline-3-carboxylic acid or 7-[3-S-(2-S-aminopropionylamino)pyrrolidin-1-yl]-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid; and calcium in an amount in the range of 0.001 % to about 1.0 % by weight of the 7-(3-amino-1-pyrrolidinyl)-8-chloro-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxoquinoline-3-carboxylic acid or 7-[3-S-(2-S-aminopropionylamino) pyrrolidin-1-yl]-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid.