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[54] **PULSATILE ONCE-A-DAY DELIVERY SYSTEMS FOR MINOCYCLINE**

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4,353,887 10/1982 Hess 424/15
 4,606,909 8/1986 Bechgaard 424/21
 4,784,858 11/1988 Ventouras 424/468
 4,837,030 6/1989 Valorose 424/456
 5,133,974 7/1992 Paradissis et al. 424/494

FOREIGN PATENT DOCUMENTS

2041222 10/1980 United Kingdom .
 0327295 9/1989 United Kingdom .
 0310814 12/1989 United Kingdom .

OTHER PUBLICATIONS

Physicians Desk Reference 1987 (43rd Ed)—Pages on Lederle Minocin—pp. 1487-1489.
 Remington's Pharmaceutical Science, 1985, 17th Ed. pp. 278-1320.

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Related U.S. Application Data

[63] Continuation of Ser. No. 410,708, Sep. 21, 1989, abandoned.

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[58] Field of Search **424/490, 452, 457, 458, 424/461, 462, 489, 494**

References Cited

U.S. PATENT DOCUMENTS

[56] 3,080,294 3/1963 Shepard 167/82
 3,148,212 9/1964 Boothe 260/559
 3,161,654 12/1964 Shen 260/319
 3,226,436 12/1965 Petisi 260/559
 3,356,571 12/1967 Takesue et al. 424/78.31
 3,499,959 3/1970 Corn 424/496
 3,865,935 2/1975 Amann 424/181
 4,138,475 2/1979 McAinsh 424/19
 4,173,626 11/1979 Dempski 424/19
 4,250,166 2/1981 Maekawa et al. 424/81

[57] ABSTRACT

Pharmaceutical delivery systems containing 7-dimethyl-6-deoxy-6-demethyltetracycline or a non-toxic acid addition salt thereof comprising mixtures or separate administration units of pH sensitive polymer coated spherical granules adapted to release the minocycline in a medium having a pH of in the range of from about 4.0 to about 7.5 and coated or uncoated quick release granules adapted to release minocycline in a medium having a pH of less than about 3.9 or minocycline powder, pH adapted multi-coated compositions and oral dosage unit form liquids, capsules or tablets containing the above are provided. These systems and formulations provide at least minimum therapeutic blood levels of minocycline for at least about 24 hours when administered to a subject only once-a-day. Methods for the preparation of the systems and formulations are provided as well.

34 Claims, 14 Drawing Sheets

