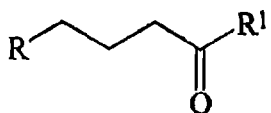




## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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| (21) International Application Number: PCT/US00/03586<br>(22) International Filing Date: 11 February 2000 (11.02.00)<br>(30) Priority Data:<br>09/251,634                  17 February 1999 (17.02.99)          US<br>(71) Applicant (for all designated States except BB US): TEVA<br>PHARMACEUTICAL INDUSTRIES, LTD. [IL/IL]; 5<br>Basel Street, P.O. Box 3190, 49131 Petah Tiqva (IL).<br>(71) Applicant (for BB only): TEVA PHARMACEUTICALS USA,<br>INC. [US/US]; 1510 Delp Drive, Kulpville, PA 19443<br>(US).<br>(72) Inventors; and<br>(75) Inventors/Applicants (for US only): LIDOR-HADAS, Ramy<br>[IL/IL]; Mor Street 19, 44242 Kfar Saba (IL). LIFSHITZ,<br>Revital [IL/IL]; 12a Kibbush Ila'avoda Street, Apartment<br>#8, Herzlia 46322 (IL).<br>(74) Agents: LEE, Steven, J. et al.; Kenyon & Kenyon, One<br>Broadway, New York, NY 10004 (US). |  | (81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG,<br>BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE,<br>ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,<br>KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,<br>MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU,<br>SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,<br>US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE,<br>LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM,<br>AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT,<br>BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU,<br>MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM,<br>GA, GN, GW, ML, MR, NE, SN, TD, TG).<br><br>Published<br>With international search report.<br><br><br>*G00001* |                                                                |
| (54) Title: NOVEL PROCESS FOR PREPARING ALENDRONIC ACID<br><br><div style="text-align: center;">  <span style="margin-left: 20px;">(I)</span> </div>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                |
| (57) Abstract<br><br>A novel process for the preparation of alendronic acid is disclosed. The method comprises the steps of reacting a compound of formula (I) with H <sub>3</sub> PO <sub>3</sub> wherein R is an imido group and R <sup>1</sup> is selected from the group consisting of chloro, bromo, iodo, fluoro, hydroxy, amino, -OR <sup>2</sup> or -OC(O)R <sup>2</sup> , wherein R <sup>2</sup> is C <sub>1</sub> -C <sub>12</sub> alkyl, C <sub>1</sub> -C <sub>12</sub> cycloalkyl or C <sub>1</sub> -C <sub>12</sub> aryl; and then reacting the product of the first step with a deprotecting agent. Alendronic acid is then recovered. The method is safe, efficient and suitable for use on a large scale.                                                                                                                                    |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                |
| <br>*162162*                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                |