



- (51) **International Patent Classification:**
C07D 257/02 (2006.01) *A61K 49/00* (2006.01)
C07F 5/00 (2006.01)
- (21) **International Application Number:**
PCT/EP2012/057013
- (22) **International Filing Date:**
17 April 2012 (17.04.2012)
- (25) **Filing Language:** English
- (26) **Publication Language:** English
- (30) **Priority Data:**
10 2011 100 128.3 21 April 2011 (21.04.2011) DE
- (71) **Applicant (for all designated States except US):** **BAYER INTELLECTUAL PROPERTY GMBH** [DE/DE]; Alfred-Nobel-Str. 10, 40789 Monheim (DE).
- (72) **Inventors; and**
- (75) **Inventors/Applicants (for US only):** **PLATZEK, Johannes** [DE/DE]; Grottkauer Str. 55, 12621 Berlin (DE). **TRENTMANN, Wilhelm** [DE/DE]; Gasselstiege 419, 48159 Münster (DE).
- (74) **Common Representative:** **BAYER INTELLECTUAL PROPERTY GMBH**; Creative Campus Monheim, Alfred-Nobel-Str. 10, 40789 Monheim (DE).

- (81) **Designated States** (*unless otherwise indicated, for every kind of national protection available*): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.
- (84) **Designated States** (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report (Art. 21(3))

(54) **Title:** PREPARATION OF HIGH-PURITY GADOBUTROL

(57) **Abstract:** What is described is a process for producing high-purity gadobutrol in a purity (according to HPLC) of more than 99.7 or 99.8 or 99.9% and the use for preparing a pharmaceutical formulation for parenteral administration. The process is carried out using specifically controlled crystallization conditions. The more recent developments in the field of the gadolinium-containing MR contrast agents (EP 0448191 B1, CA Patent 1341176, EP 0643705 B1, EP 0986548 B1, EP 0596586 B1) include the MRT contrast agent gadobutrol (Gadovist® 1.0) which has been approved for a relatively long time in Europe and more recently also in the USA under the name Gadavist®.



WO 2012/143355 A1