# Product Data Sheet

Product Name: Digeranyl bisphosphonate
Cat. No.: GC65270

## Chemical Properties

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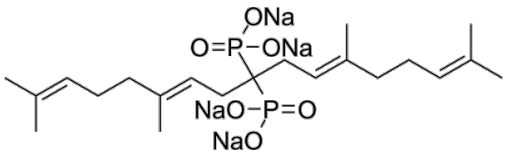
| Cas. No. | 878143-03-4 | | |
| Formula | $C_{21}H_{34}Na_4O_6P_2$ | M.Wt | 536.4 |
| Solubility | DMSO : 2 mg/mL (3.73 mM; Need ultrasonic)\|Water : 2 mg/mL (3.73 mM; Need ultrasonic) | Storage | Store at -20°C, protect from light, stored under nitrogen |
| General tips | For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months. | | |
| Shipping Condition | Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request. | | |
| Structure | | | |




## Protocol

*Caution: Product has not been fully validated for medical applications. For research use only.*
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# Product Data Sheet

| **Cell experiment [1]:** | |
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| Cell lines | LNCaP cells (human prostate adenocarcinoma cell line), 22Rv1 cells (human prostate cancer cell line), C4-2B4 cells (human prostate cancer cell line) |
| Preparation Method | LNCaP, 22Rv1 and C4-2B4 cells were cultured in RPMI-1640 with 10% FBS at 37°C, 5% $CO_2$. For AR localization, cells on coverslips were treated with 30μM Digeranyl bisphosphonate for 72h, then fixed and stained with anti-AR/DAPI/ActinGreen for deconvolution microscopy. For ARE-luciferase, LNCaP-ARE-luc and 22Rv1-ARE-luc cells were treated with Digeranyl bisphosphonate for 72h in 3% charcoal-stripped FBS media with 1nM R1881 for last 24h, then lysed for luciferin readout. For AR target genes, LNCaP cells were treated with 30μM Digeranyl bisphosphonate for 48h plus 1nM R1881, then harvested for RT-qPCR of FKBP5, KLK3, NKX3-1, TMPRSS2. For NEPC phenotype, LNCaP cells were co-treated with 2.5μM Digeranyl bisphosphonate in steroid-reduced media for 28 days, then assessed by Western blot (AR, CgA, NSE) and projection counting. |
| Reaction Conditions | 30μM; 48h-28 days |
| Applications | Digeranyl bisphosphonate reduced ARE-luciferase reporter activity in LNCaP-ARE-luc and 22Rv1-ARE-luc cells. Digeranyl bisphosphonate reduced R1881-induced mRNA levels of FKBP5, KLK3, NKX3-1 and TMPRSS2 in LNCaP cells. Digeranyl bisphosphonate decreased nuclear localization of AR in LNCaP, 22Rv1 and C4-2B4 cells. Digeranyl bisphosphonate reduced AR, CgA and NSE protein levels in steroid-reduced LNCaP cells over 28 days. Digeranyl bisphosphonate reduced cellular projection number and maintained epithelial-like morphology in steroid-reduced LNCaP cells. |
| **Animal experiment [2]:** | |

# Product Data Sheet

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| Animal models | 8-week-old male C57BL/6J mice |
| Preparation Method | Mice received subcutaneous injection of 0.15mg/kg Digeranyl bisphosphonate (DGBP) twice daily for 5 consecutive days before surgery. On day 6, mice underwent ligation of common bile duct and cholecystectomy (BDLC). Mice were sacrificed 5 days after BDLC. Liver FPP, GGPP, FOH, GGOH were measured by LC/MS; serum ALT, TB, TBA by biochemical assay; liver morphology by stereomicroscopy; necrosis by H&E staining; overall survival by Kaplan-Meier. |
| Dosage form | 0.15mg/kg; subcutaneous; twice daily for 5 days |
| Applications | Digeranyl bisphosphonate elevated hepatic FPP and FOH levels. Digeranyl bisphosphonate improved overall survival after BDLC. Digeranyl bisphosphonate maintained physiologically normal liver morphology after BDLC. Digeranyl bisphosphonate reduced serum ALT, total bilirubin and total bile acid levels. Digeranyl bisphosphonate decreased liver necrotic area after BDLC. |

References:

[1] Weissenrieder JS, Reilly JE, Neighbors JD, et al. Inhibiting geranylgeranyl diphosphate synthesis reduces nuclear androgen receptor signaling and neuroendocrine differentiation in prostate cancer cell models. Prostate. 2018;1-10.

[2] Jia WJ, Tang QL, Jiang S, et al. Conditional loss of geranylgeranyl diphosphate synthase alleviates acute obstructive cholestatic liver injury by regulating hepatic bile acid metabolism. FEBS J. 2020;287(1):1-18.

## Background

# Product Data Sheet

Digeranyl bisphosphonate is a lipophilic geranylgeranyl diphosphate synthase (GGDPS) inhibitor. Digeranyl bisphosphonate competitively binds to the GGDPS active site. Digeranyl bisphosphonate attenuates Rac1 mitochondrial import, mitochondrial oxidative stress, ERK phosphorylation, and caspase activation. Digeranyl bisphosphonate induces apoptosis or autophagy. Digeranyl bisphosphonate can be used in studies related to pulmonary fibrosis, lymphoid leukemia, prostate cancer metastasis, and multiple myeloma[1-4].

In vitro, treatment of Molt-4 cells with 15-30μM Digeranyl bisphosphonate for 72 hours, or treatment of Jurkat cells with 30μM or 81μM Digeranyl bisphosphonate for 72 hours, dose-dependently inhibited cell proliferation and increased the proportion of late apoptotic cells[5]. Treatment of LNCaP cells with 30μM Digeranyl bisphosphonate for 48 hours to 28 days reduced mRNA expression of FKBP5, KLK3, NKX3-1, and TMPRSS2. Treatment of LNCaP, 22Rv1, and C4-2B4 cells with Digeranyl bisphosphonate for 72 hours reduced AR nuclear localization[6]. Treatment of MDA-MB-231 human breast cancer cells with 25μM Digeranyl bisphosphonate for 24 hours reduced membrane-associated RhoA, increased cytosolic RhoA, and increased GTP-bound RhoA. Treatment of MDA-MB-231 cells with 25μM Digeranyl bisphosphonate for 24 hours or continuously for up to 71 hours inhibited cell transwell migration and time-dependently reduced cell migration speed[7].

In vivo, C57BL/6 wild-type mice received subcutaneous implantation of osmotic pumps containing 0.2mg/kg Digeranyl bisphosphonate. The next day, mice received intratracheal administration of 100μg Chrysotile or 1.3-2.0U/kg Bleomycin Sulfate. Continuous drug delivery lasted 21 days. Digeranyl bisphosphonate reduced mitochondrial Rac1 content and increased cytosolic Rac1 in alveolar macrophages. Digeranyl bisphosphonate reduced reactive oxygen species generation rate in mitochondrial. Seven days after Bleomycin administration, osmotic pumps containing 0.2mg/kg Digeranyl bisphosphonate were implanted for another 21 days. Digeranyl bisphosphonate reduced lung hydroxyproline content, significantly decreased collagen plaque area, and prevented pulmonary fibrosis progression[8]. Starting 5 days before bile duct ligation and cholecystectomy (BDLC), C57BL/6J mice received subcutaneous injections of 0.15mg/kg Digeranyl bisphosphonate twice daily for 5 consecutive days. Mice then underwent BDLC and were sacrificed on day 5 after surgery. Digeranyl bisphosphonate improved overall survival rate at 5 days after surgery, reduced serum ALT, total bilirubin, and total bile acid levels, decreased liver necrotic area, and alleviated acute obstructive cholestatic liver injury[9]. Metabolically unhealthy obesity (MUO) model C57BL/6J mice received subcutaneous injections of 0.15mg/kg Digeranyl bisphosphonate for 5 consecutive days. Digeranyl

bisphosphonate improved glucose tolerance and insulin sensitivity, reduced plasma glucose and insulin concentrations, and alleviated hepatic lipid deposition. Body weight and liver weight were not changed. Serum ALT and AST levels were elevated[10].

References:

[1] Wiemer AJ, Tong H, Swanson KM, et al. Digeranyl bisphosphonate inhibits geranylgeranyl pyrophosphate synthase. Biochem Biophys Res Commun. 2007 Feb 23;353(4):921-5.

[2] Wasko BM, Dudakovic A, Hohl RJ. Bisphosphonates induce autophagy by depleting geranylgeranyl diphosphate. J Pharmacol Exp Ther. 2011 May;337(2):540-6.

[3] Weivoda MM, Hohl RJ. The effects of direct inhibition of geranylgeranyl pyrophosphate synthase on osteoblast differentiation. J Cell Biochem. 2011 Jun;112(6):1506-13.

[4] Haney SL, Wills VS, Wiemer DF, et al. Recent Advances in the Development of Mammalian Geranylgeranyl Diphosphate Synthase Inhibitors. Molecules. 2017 May 27;22(6):886.

[5] Agabiti SS, Li J, Wiemer AJ. Geranylgeranyl diphosphate synthase inhibition induces apoptosis that is dependent upon GGPP depletion, ERK phosphorylation and caspase activation. Cell Death Dis. 2017;8(3):e2678.

[6] Weissenrieder JS, Reilly JE, Neighbors JD, et al. Inhibiting geranylgeranyl diphosphate synthesis reduces nuclear androgen receptor signaling and neuroendocrine differentiation in prostate cancer cell models. Prostate. 2018;1-10.

[7] Dudakovic A, Tong H, Hohl RJ. Geranylgeranyl diphosphate depletion inhibits breast cancer cell migration. Invest New Drugs. 2011;29(5):912-920.

[8] Osborn-Heaford HL, Murthy S, Gu L, et al. Targeting the isoprenoid pathway to abrogate progression of pulmonary fibrosis. Free Radic Biol Med. 2015 Sep;86:47-56.

[9] Jia WJ, Tang QL, Jiang S, et al. Conditional loss of geranylgeranyl diphosphate synthase alleviates acute obstructive cholestatic liver injury by regulating hepatic bile acid metabolism. FEBS J. 2020;287(1):1-18.

[10] Zhao Y, Nie HY, Jiang S, et al. Geranylgeranyl Pyrophosphate Promotes Hepatic Lipid

# Product Data Sheet

Accumulation by Prenylation of Perilipin4. Cell Mol Gastroenterol Hepatol. 2025;19:101546.