# Product Data Sheet

Product Name: DOXO-EMCH
Cat. No.: GC15250

## Chemical Properties

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|---|---|---|---|
| Cas. No. | 151038-96-9 | | |
| Chemical Name | N-[(Z)-[1-[(2S,4S)-4-[(2R,4S,5S,6S)-4-amino-5-hydroxy-6-methyloxan-2-yl]oxy-2,5,12-trihydroxy-7-methoxy-6,11-dioxo-3,4-dihydro-1H-tetracen-2-yl]-2-hydroxyethylidene]amino]-6-(2,5-dioxopyrrol-1-yl)hexanamide | | |
| SMILES | CC1C(C(CC(O1)OC2CC(CC3=C(C4=C(C(=C23)O)C(=O)C5=C(C4=O)C=CC=C5OC)O)(C(=NNC(=O)CCCCCN6C(=O)C=CC6=O)CO)O)N)O | | |
| Formula | $C_{37}H_{42}N_4O_{13}$ | M.Wt | 750.75 |
| Solubility | Soluble in DMSO | Storage | Store at -20°C |
| General tips | For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ 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 | DOXO-EMCH | | |

## Protocol

### Cell experiment [1]:

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| Cell lines | Human multiple myeloma cell lines RPMI8226 and U266 |
| Preparation method | Soluble in DMSO. General tips for obtaining a higher concentration: Please warm the tube at 37 ℃ for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20℃ for several months. |
| Reacting condition | 0.27-2.16 mmol/L, 48 hours |


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| Applications | INNO-206 inhibited blood vessel formation and reduced multiple myeloma cell growth in a pH-dependent fashion. In RPMI8226 cells, INNO-206 decreased cell viability in concentration-and pH-dependent manner. At pH5, INNO-206≥0.54 mmol/Lessentially eliminated cell viability. In the MM1S cell line, INNO-206 inhibited cell growth in concentration and pH-dependent manner. |

**Animal experiment [1, 2]:**

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| Animal models | Mice bearing the LAGk-1A tumor, multiple myeloma xenograft(LAGk-2) mouse model |
| Dosage form | Intravenous injection, 10.8 mg/kg; 3 times weekly at 1.8 mg/kg; once weekly at 5.4 mg/kg |
| Application | In mice bearing the LAGk-1A tumor, INNO-206 (10.8 mg/kg, once weekly, i.v.) showed significantly smaller tumor volumes and IgG levels on days 28, 35 and 42. In LAGk-2–bearing mice, treatment with INNO-206 (i.v. 3 times weekly at 1.8 mg/kg) significantly reduced tumor volume. INNO-206 (once weekly, 5.4 mg/kg) showed significantly smaller tumor volumes. |
| Other notes | Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal. |


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References:

[1]. Sanchez E, Li M, Wang C, et al. Anti-myeloma effects of the novel anthracycline derivative INNO-206[J]. Clinical Cancer Research, 2012, 18(14): 3856-3867.

[2]. Graeser R, Esser N, Unger H, et al. INNO-206, the (6-maleimidocaproyl hydrazone derivative of doxorubicin), shows superior antitumor efficacy compared to doxorubicin in different tumor xenograft models and in an orthotopic pancreas carcinoma model[J]. Investigational new drugs, 2010, 28(1): 14-19.

## Background

The (6-maleimidocaproyl) hydrazone derivative of doxorubicin (INNO-206), formerly known as DOXO-EMCH, is a prodrug of the anticancer agent doxorubicin which selectively binds to the cys34 of circulating albumin and accumulates in solid tumors due to passive targeting[1]. INNO-206 shows significantly superior antitumor efficacy over free doxorubicin in a spectrum of preclinical tumor models [2].

In vivo: In a murine renal cell carcinoma model and in breast carcinoma xenograft models, INNO-206 has shown superior activity over doxorubicin. INNO-206 has shown more potent antitumor efficacy than free doxorubicin in the tumor models and is thus a promising clinical candidate for treating a broad range of solid tumors [2].

Clinical trials: In a phase I study, INNO-206 showed a good safety profile at doses up to 260 mg/m2 doxorubicin equivalents. INNO-206 was able to induce tumor regressions in breast cancer, small cell lung cancer and sarcoma. [1].

References:
[1]. Kratz F. DOXO-EMCH (INNO-206): the first albumin-binding prodrug of doxorubicin to enter clinical trials[J]. Expert opinion on investigational drugs, 2007, 16(6): 855-866.
[2]. Graeser R, Esser N, Unger H, et al. INNO-206, the (6-maleimidocaproyl hydrazone

derivative of doxorubicin), shows superior antitumor efficacy compared to doxorubicin in different tumor xenograft models and in an orthotopic pancreas carcinoma model[J]. Investigational new drugs, 2010, 28(1): 14-19.
[3]. Graeser R, Esser N, Unger H, et al. INNO-206, the (6-maleimidocaproyl hydrazone derivative of doxorubicin), shows superior antitumor efficacy compared to doxorubicin in different tumor xenograft models and in an orthotopic pancreas carcinoma model[J]. Investigational new drugs, 2010, 28(1): 14-19.


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