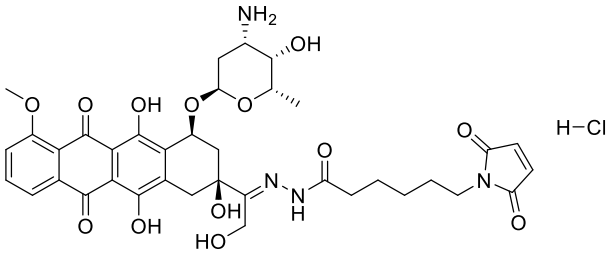
Product data sheet

MedKoo Cat#: 201550 Name: Aldoxorubicin HCl CAS#: 480998-12-7 (HCl) Chemical Formula: $C_{37}H_{43}ClN_4O_{13}$ Molecular Weight: 787.25	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

Aldoxorubicin, also known as INNO-206 and Doxo-EMCH, is the 6-maleimidocaproyl hydrazone derivative prodrug of the anthracycline antibiotic doxorubicin with antineoplastic activity. INNO-206 binds selectively to the cysteine-34 position of albumin via its maleimide moiety. Doxorubicin is released from the albumin carrier after cleavage of the acid-sensitive hydrazone linker within the acidic environment of tumors and, once located intracellularly, intercalates DNA, inhibits DNA synthesis, and induces apoptosis. Albumin tends to accumulate in solid tumors as a result of high metabolic turnover, rapid angiogenesis, hyervasculature, and impaired lymphatic drainage. Because of passive accumulation within tumors, this agent may improve the therapeutic effects of doxorubicin while minimizing systemic toxicity.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	6.0	20.3

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	3.39 mL	16.93 mL	33.86 mL
5 mM	0.68 mL	3.39 mL	6.77 mL
10 mM	0.34 mL	1.69 mL	3.39 mL
50 mM	0.07 mL	0.34 mL	0.68 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Sanchez E, Li M, Wang C, Nichols CM, Li J, Chen H, Berenson JR. Anti-myeloma effects of the novel anthracycline derivative INNO-206. Clin Cancer Res. 2012 Jul 15;18(14):3856-67. doi: 10.1158/1078-0432.CCR-11-3130. Epub 2012 May 22. PMID: 22619306.

In vivo study

1. Sanchez E, Li M, Wang C, Nichols CM, Li J, Chen H, Berenson JR. Anti-myeloma effects of the novel anthracycline derivative INNO-206. Clin Cancer Res. 2012 Jul 15;18(14):3856-67. doi: 10.1158/1078-0432.CCR-11-3130. Epub 2012 May 22. PMID: 22619306.

2. Graeser R, Esser N, Unger H, Fichtner I, Zhu A, Unger C, Kratz F. 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. Invest New Drugs. 2010 Feb;28(1):14-9. doi: 10.1007/s10637-008-9208-2. Epub 2009 Jan 8. PMID: 19148580.

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7. Bioactivity

Biological target:

Aldoxorubicin (INNO-206) is an albumin-binding prodrug of Doxorubicin (DNA topoisomerase II inhibitor), which is released from albumin under acidic conditions.

In vitro activity

Because INNO-206 shows that the highest level of releasing doxorubicin is at pH 5, the cytotoxicity of INNO-206 or doxorubicin was assessed in a concentration- and pH-dependent fashion in the 3 multiple myeloma cell lines RPMI8226, U266, and MM1S. First, drugs were prepared in pH 5 or 7 for 45 minutes before their addition to the cell culture. To compare equivalent concentrations of doxorubicin-bound INNO-206 to free doxorubicin, the INNO-206 concentrations were divided by 1.346 as this gives the amount of free doxorubicin contained within the INNO-206 compound. Cells were then exposed to increasing concentrations of INNO-206 from 0.27 to 2.16 μmol/L (free doxorubicin equivalent doses of 0.2–1.6 μmol/L) or doxorubicin (0.2–1.6 μmol/L) for 48 hours, and cell viability was determined with the MTS assay. A concentration- and pH-dependent decrease in viable RPMI8226 cells was observed after exposure to INNO-206 or doxorubicin (Fig. 1A). At pH 5, viable cells were essentially eliminated in cells cultured with INNO-206 at concentrations $\geqslant$0.54 μ mol/L and doxorubicin was also effective but less so than INNO-206 (Fig. 1A). A similar concentration and pH-dependent inhibition of cell growth, as those observed earlier, was observed in the MM1S cell line after exposure to INNO-206 or doxorubicin (Fig. 1B). As the concentration was increased and pH was decreased, from pH 7 to 5, the percentage of viable MM1S cells within the INNO-206 group dramatically decreased, in contrast to what occurred with doxorubicin. In fact, the anti–multiple myeloma effects of doxorubicin at 0.4 and 0.8 μmol/L were less at pH 5 than 7. The diminishing anti–multiple myeloma effects of doxorubicin in an acidic environment were also observed in the U266 cell line (Fig. 1C), in contrast to INNO-206 where increased anti–multiple myeloma effects were observed at the lower pH. Because the data above was generated from drugs incubated at physiologic pH and at pH 5, the effect of an acidic pH alone on multiple myeloma cell lines was also tested. Exposure of multiple myeloma cells to pH 5 only resulted in a minimal reduction in viable cells compared to those cultured at pH 7. A representative example from all 3 cell lines tested is shown in Fig. 1D.

Reference: Clin Cancer Res. 2012 Jul 15;18(14):3856-67.
http://clincancerres.aacrjournals.org/cgi/pmidlookup?view=long&pmid=22619306

In vivo activity

Mice bearing the LAGκ-1A tumor receiving INNO-206 once weekly via i.v. injection at 10.8 mg/kg (equivalent to 8.0 mg/kg of doxorubicin) showed significantly smaller tumor volumes and IgG levels on days 28 (tumor volumes: P = 0.0152; hIgG: P = 0.0019), 35 (tumor volumes: P = 0.0051; hIgG: P = 0.0006) and 42 (tumor volumes: P = 0.0036; hIgG: P = 0.0113) compared with vehicle—treated mice (Fig. 3A and B). This INNO-206 treatment regimen was well tolerated with 90% of mice surviving until the termination of the study (day 42).

Reference: Clin Cancer Res. 2012 Jul 15;18(14):3856-67.
http://clincancerres.aacrjournals.org/cgi/pmidlookup?view=long&pmid=22619306

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.