# Product data sheet

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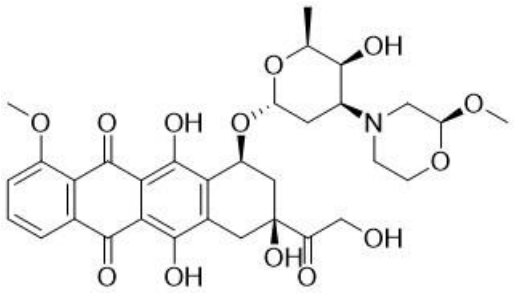
|---|---|
| MedKoo Cat#: 201824<br>Name: Nemorubicin<br>CAS#: 108852-90-0<br>Chemical Formula: $C_{32}H_{37}NO_{13}$<br>Exact Mass: 643.22649<br>Molecular Weight: 643.63 |  |
| Product supplied as: | Powder |
| Purity (by HPLC): | ≥ 98% |
| Shipping conditions | Ambient temperature |
| Storage conditions: | Powder: -20°C 3 years; 4°C 2 years. |
| | In solvent: -80°C 3 months; -20°C 2 weeks. |

**1. Product description:**

Nemorubicin, also known as PNU152243A, is a doxorubicin derivative that differs significantly from its parent drug in terms of spectrum of antitumor activity, metabolism and toxicity profile. The drug is active on tumors resistant to alkylating agents, topoisomerase II inhibitors and platinum derivatives. It works primarily through topoisomerase I inhibition. Of note, Nemorubicin is active in cells with upregulation of the nucleotide excision repair (NER) pathway, where current therapies fail. Nemorubicin is biotransformed in the liver into cytotoxic metabolites that may further contribute to render this drug highly active against primary liver tumors or liver metastases.

**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 | 60.0 | 101.0 |

**4. Stock solution preparation table:**

| Concentration / Solvent Volume / Mass | 1 mg | 5 mg | 10 mg |
|---|---|---|---|
| 1 mM | 1.55 | 7.77 | 15.54 |
| 5 mM | 0.31 | 1.55 | 3.11 |
| 10 mM | 0.16 | 0.78 | 1.55 |
| 50 mM | 0.03 | 0.16 | 0.31 |

**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. Quintieri L, Geroni C, Fantin M, Battaglia R, Rosato A, Speed W, Zanovello P, Floreani M. Formation and antitumor activity of PNU-159682, a major metabolite of nemorubicin in human liver microsomes. Clin Cancer Res. 2005 Feb 15;11(4):1608-17. doi: 10.1158/1078-0432.CCR-04-1845. PMID: 15746066.
2. Quintieri L, Fantin M, Palatini P, De Martin S, Rosato A, Caruso M, Geroni C, Floreani M. In vitro hepatic conversion of the anticancer agent nemorubicin to its active metabolite PNU-159682 in mice, rats and dogs: a comparison with human liver microsomes. Biochem Pharmacol. 2008 Sep 15;76(6):784-95. doi: 10.1016/j.bcp.2008.07.003. Epub 2008 Jul 11. PMID: 18671948.

In vivo study

1. Broggini M. Nemorubicin. Top Curr Chem. 2008;283:191-206. doi: 10.1007/128_2007_6. PMID: 23605633.
2. Lu H, Chen CS, Waxman DJ. Potentiation of methoxymorpholinyl doxorubicin antitumor activity by P450 3A4 gene transfer. Cancer Gene Ther. 2009 May;16(5):393-404. doi: 10.1038/cgt.2008.93. Epub 2008 Nov 14. PMID: 19011599; PMCID: PMC2669851.

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**7. Bioactivity**

Biological target:

Nemorubicin (Methoxymorpholinyl doxorubicin) is a Doxorubicin derivative with potent antitumor activity and IC70s of 578 nM, 468 nM, 193 nM, 191 nM, 68 nM.

In vitro activity

The aims of this study were to obtain information about MMDX biotransformation to PNU-159682 in humans, and to explore the antitumor activity of PNU-159682. The cytotoxicity and antitumor activity of PNU-159682 was examined using a panel of in vitro-cultured human tumor cell lines and tumor-bearing mice, respectively. HLMs converted MMDX to a major metabolite, whose retention time in liquid chromatography and ion fragmentation in tandem mass spectrometry were identical to those of synthetic PNU-159682. In a bank of HLMs from 10 donors, rates of PNU-159682 formation correlated significantly with three distinct CYP3A-mediated activities. Troleandomycin and ketoconazole, both inhibitors of CYP3A, markedly reduced PNU-159682 formation by HLMs; the reaction was also concentration-dependently inhibited by a monoclonal antibody to CYP3A4/5. Of the 10 cDNA-expressed CYPs examined, only CYP3A4 formed PNU-159682. In addition, PNU-159682 was remarkably more cytotoxic than MMDX and doxorubicin in vitro.

Clin Cancer Res. 2005 Feb 15;11(4):1608-17. https://pubmed.ncbi.nlm.nih.gov/15746066/

In vivo activity

This study investigated methoxymorpholinyl-doxorubicin (MMDX), a novel CYP3A-activated anticancer prodrug. 9L and 9L/3A4 tumors were implanted s.c. and grown in male scid mice. Tumor vol (A) and body weight (B) were measured twice a week. In the absence of drug treatment, 9L/3A4 tumors grew somewhat slower than 9L tumors (doubling time of 5.8 d vs. 4.6 d; Table 2). Arrows indicate days on which each of three weekly doses of MMDX (60 μg/kg) was administered, either by i.v. or i.t. injection, as indicated, beginning when the tumors reached 300–400 mm3 in size. MMDX was highly toxic by the i.v. administration route, with 4 out of 4 i.v. injected 9L tumor-bearing mice dying by day 21 (i.e., 7 d after completing the cycle of three weekly MMDX injections), and 3 out of 4 i.v. MMDX-injected 9L/3A4 tumor-bearing mice dying by day 24. Drug toxicity was not observed for the i.t. MMDX 9L/3A4 tumor group until after completion of a second cycle of three weekly MMDX injections, with 1 mouse dying on day 52 and a second mouse on day 56. Notably, intratumoral expression of CYP3A4 increased MMDX antitumor activity dramatically, even though MMDX itself has substantial intrinsic anticancer activity, and despite the fact that MMDX-activating CYP3A enzymes are already expressed endogenously at a high level in mouse liver , as they are in human liver . The strong chemosensitization of 9L/3A4 tumors to MMDX reported here further suggests that MMDX may be particularly active against tumors that express CYP3A4 endogenously, i.e., without the introduction of a gene therapy vector.

Cancer Gene Ther. 2009 May; 16(5): 393–404. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2669851/