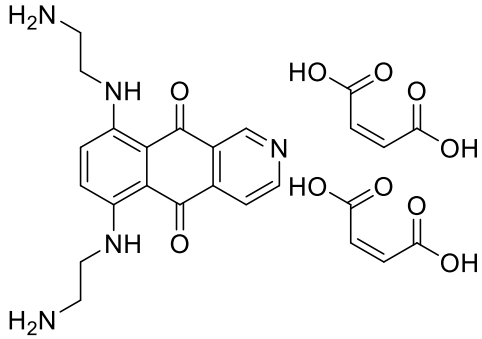
Product data sheet

MedKoo Cat#: 202250 Name: Pixantrone Maleate CAS#: 144675-97-8 (maleate) Chemical Formula: $C_{25}H_{27}N_5O_{10}$ Molecular Weight: 557.52	
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:
Pixantrone is a synthetic, noncardiotoxic aza-anthracenedione analogue with potential antineoplastic activity. Pixantrone intercalates into DNA and induces topoisomerase II-mediated DNA strand crosslinks, resulting in inhibition of DNA replication and tumor cell cytotoxicity. Pixantrone is a potentially more effective, less cardiotoxic alternative to doxorubicin for patients with aggressive non-Hodgkin lymphoma (aNHL).

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	30.0	53.8
H2O	5.0	9.0

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.79 mL	8.97 mL	17.94 mL
5 mM	0.36 mL	1.79 mL	3.59 mL
10 mM	0.18 mL	0.90 mL	1.79 mL
50 mM	0.04 mL	0.18 mL	0.36 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. Willenbacher E, Jöhrer K, Willenbacher W, Flögel B, Greil R, Kircher B. Pixantrone demonstrates significant in vitro activity against multiple myeloma and plasma cell leukemia. Ann Hematol. 2019 Nov;98(11):2569-2578. doi: 10.1007/s00277-019-03797-6. Epub 2019 Oct 18. PMID: 31628518; PMCID: PMC6848044.
2. Beeharry N, Di Rora AG, Smith MR, Yen TJ. Pixantrone induces cell death through mitotic perturbations and subsequent aberrant cell divisions. Cancer Biol Ther. 2015;16(9):1397-406. doi: 10.1080/15384047.2015.1070979. PMID: 26177126; PMCID: PMC4621998.

In vivo study

1. Kurmasheva RT, Reynolds CP, Kang MH, Allievi C, Houghton PJ, Smith MA. Initial testing (stage 1) of the topoisomerase II inhibitor pixantrone, by the pediatric preclinical testing program. Pediatr Blood Cancer. 2014 May;61(5):922-4. doi: 10.1002/pbc.24800. Epub 2013 Oct 26. PMID: 24166988; PMCID: PMC3951603.
2. Ubiali F, Nava S, Nessi V, Longhi R, Pezzoni G, Capobianco R, Mantegazza R, Antozzi C, Baggi F. Pixantrone (BBR2778) reduces the severity of experimental autoimmune myasthenia gravis in Lewis rats. J Immunol. 2008 Feb 15;180(4):2696-703. doi: 10.4049/jimmunol.180.4.2696. PMID: 18250482.

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7. Bioactivity

Biological target:

Pixantrone dimaleate is a topoisomerase II inhibitor and DNA intercalator, with anti-tumor activity.

In vitro activity

To test whether the strong anti-proliferative activity of PIX (pixantrone) resulted also in cytotoxicity, the metabolic activity of mitochondria of the myeloma cell lines was measured after 72 h of incubation with PIX in comparison to Dox. PIX dose-dependently inhibited the metabolic activity of myeloma cell lines (Fig.2a). The IC50 for the inhibition was cell line-dependent and in the range of 0.5–5 μM. The cell lines AMO-1 and KMS-12-BM (IC50 at 0.5 μM) were more sensitive to PIX treatment than the other cell lines. To further evaluate the cytotoxic activity, flow cytometry analyses were performed 48 h and 7 days after PIX treatment. After 48 h, a concentration of 0.25 μM PIX reduced the viability of the cell line KMS-12-BM to 75.3 ± 5.4%, whereas 5 μM decreased it to 45.4 ± 6.7% (data not shown). Apoptosis induction, however, was observed only after a 7-day incubation (Fig.33). The ability of PIX to induce cell death of primary plasma cells from patients was assessed after a 24-h incubation period in vitro. PIX dose-dependently diminished the extent of the cells alive of two patients with refractory relapsed MM (multiple myeloma) and five patients with de-novo or secondary PCL. At 2.5 μM, the proportion of plasma cells alive was reduced to 67.9 ± 10.4% of control without PIX (Fig.5a). From these data, we conclude that systematic investigations of the clinical usefulness of pixantrone in the framework of controlled clinical trials are clearly indicated.

Reference: Ann Hematol. 2019; 98(11): 2569–2578. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6848044/

In vivo activity

Pixantrone was tested against eight PPTP solid tumor xenografts using a dose of 7.5 mg/kg administered intravenously q4d x 3. This dose was based on toxicity testing in non-tumored SCID mice. The planned treatment and observation period was 6 weeks. Toxicity was not observed in either treated or control groups at the 7.5 mg/kg dose. Eight of 8 tested xenograft models were considered evaluable for efficacy. Pixantrone induced significant differences in event free survival (EFS) distribution compared to control in 25% (2 of 8) of the evaluable solid tumor xenografts, Table II. Pixantrone induced tumor growth inhibition meeting criteria for intermediate EFS T/C activity in 12.5% (1 of 8) evaluable solid tumor xenografts. An objective response (KT-10, Wilms tumor) was observed in 1 of 8 solid tumor xenografts. In summary, pixantrone showed tumor regressing activity against a Wilms tumor xenograft.

Reference: Pediatr Blood Cancer. 2014 May; 61(5): 922–924. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3951603/