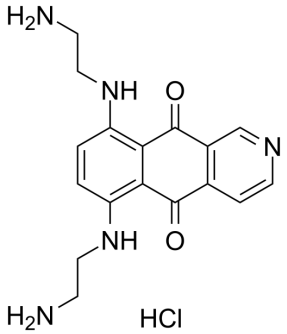
Pixantrone hydrochloride

Cat. No.:	HY-13727B
CAS No.:	175989-38-5
Molecular Formula:	$C_{17}H_{20}ClN_5O_2$
Molecular Weight:	361.83
Target:	Topoisomerase
Pathway:	Cell Cycle/DNA Damage
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	Pixantrone (BBR 2778 (free base)) hydrochloride, a mitoxantrone analog, is a topoisomerase II inhibitor and DNA intercalator, with anti-tumor activity[1][2].
IC_{50} & Target	Topoisomerase II

In Vitro

Pixantrone (0-10 μM, 72 h) hydrochloride induces cell death in multiple cancer cell lines independent of cell cycle perturbation[1].

Pixantrone (25-500 nM, 24 h) hydrochloride can induce DNA damage, hinder chromosome segregation, and induce severe chromosomal aberrations and mitotic catastrophes in PANC1 cells[1].

Pixantrone (0-100 μM, 72 h) hydrochloride potently inhibits growth of human leukemia K562 cells, etoposide-resistant K/VP.5 cells, MDCK and ABCB1-transfected MDCK/MDR cells with IC_{50}s of 0.10 μM, 0.56 μM, 0.058 μM and 4.5 μM, respectively [2].

Pixantrone (0.01-0.2 μM) hydrochloride leads to a concentration-dependent formation of linear DNA through acting on topoisomerase IIα and produces semiquinone free radicals in an enzymatic reducing system, although not in a cellular system, most likely due to low cellular uptake[2].

Pixantrone (0.01-10 μM) hydrochloride shows potent inhibitory activities against rat 97-116 peptide-specific T cell proliferation[4].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	T47D, MCF-10A and OVCAR5 cells
Concentration:	0-10 μM
Incubation Time:	72 h
Result:	Reduced the proliferation of T47D, MCF-10A and OVCAR5 cells with 37.3 nM, 126 nM and 136 nM, respectively.

Cell Proliferation Assay[4]

Cell Line:	Lewis rat T cell lines
Concentration:	0.01-10 μM

	Incubation Time:	
	Result:	Inhibited 39.3% rat 97-116 peptide-specific T cells proliferation at 0.01 μM and completely suppressed T cell proliferation at high concentrations.

In Vivo

Pixantrone (i.v., 27 mg/kg, every 7 days, three times) hydrochloride does not worsen pre-existing moderate degenerative cardiomyopathy, causes minimal cardiotoxic in mice following repeated treatment cycles and results in less mortality than mitoxantrone in doxorubicin-pretreated mice[3].

Pixantrone (i.v., 16.25 mg/kg, every week, three times) hydrochloride modulates Lymph node cells (LNC) responses, affacts T cell subpopulations in TAChR-immunized Lewis rats and also shows preventive and therapeutic effect in experimental autoimmune myasthenia gravis (EAMG) rats[4].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- J Mol Med (Berl). 2019 Aug;97(8):1183-1193.
- Methods Mol Biol. 2018;1711:351-398.

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REFERENCES

[1]. Neil Beeharry, et al. Pixantrone induces cell death through mitotic perturbations and subsequent aberrant cell divisions. Cancer Biol Ther. 2015;16(9):1397-406.

[2]. Brian B Hasinoff, et al. Mechanisms of Action and Reduced Cardiotoxicity of Pixantrone; a Topoisomerase II Targeting Agent with Cellular Selectivity for the Topoisomerase IIα Isoform. J Pharmacol Exp Ther. 2016 Feb;356(2):397-409.

[3]. Ennio Cavalletti, et al. Pixantrone (BBR 2778) has reduced cardiotoxic potential in mice pretreated with doxorubicin: comparative studies against doxorubicin and mitoxantrone. Invest New Drugs. 2007 Jun;25(3):187-95.

[4]. Federica Ubiali, et al. Pixantrone (BBR2778) reduces the severity of experimental autoimmune myasthenia gravis in Lewis rats. J Immunol. 2008 Feb 15;180(4):2696-703.

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