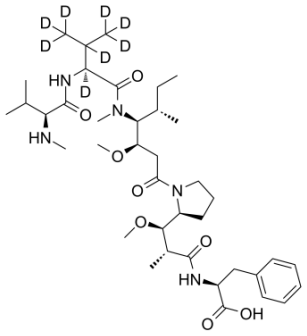
D8-MMAF

Cat. No.:	HY-15579S
Molecular Formula:	$C_{39}H_{57}D_8N_5O_8$
Molecular Weight:	740.01
Target:	Microtubule/Tubulin; ADC Cytotoxin
Pathway:	Cell Cycle/DNA Damage; Cytoskeleton; Antibody-drug Conjugate/ADC Related
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	D8-MMAF hydrochloride is a deuterated form of MMAF hydrochloride. MMAF Hydrochloride, a potent tubulin polymerization inhibitor, is used as a antitumor agent and a cytotoxic component of antibody-drug conjugates (ADCs)[1].
IC_{50} & Target	Auristatin
In Vitro	MMAF shows in vitro cytotoxicity against a panel of cell lines. The IC_{50} values for Karpas 299, H3396, 786-O and Caki-1 are 119, 105, 257, and 200 nM, respectively. Targeted MMAF is much more potent than the free drug, and that cAC10 conjugates of MMAF display pronounced activities. On a molar basis, the cAC10-L1-$MMAF_4$ is an average of over 2200-fold more potent than free MMAF and is active on all the CD30-positive cell lines tested[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	The maximum tolerated dose in mice of MMAF (>16 mg/kg) is much higher than MMAE (1 mg/kg). cAC10-L1-$MMAF_4$ has an MTD of 50 mg/kg in mice and 15 mg/kg in rats. The corresponding cAC10-L4-$MMAF_4$ ADC was much less toxic, having MTDs in mice and rats of >150 mg/ kg and 90 mg/kg in rats, respectively[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Cells are treated with serial dilutions of test molecules and incubated 4-6 days depending on cell line. Assessment of cellular growth and data reduction to generate IC_{50} values is done using Alamar Blue dye reduction assay[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice: When subcutaneous Karpas 299 tumor size reaches 300 mm^3, three animals per group receives one injection of 10 mg antibody component/kg body weight of either cAC10-L1-$MMAF_4$ or cBR96-L1-$MMAF_4$ intravenously. Tumors are then removed and placed in optimal cutting temperature compound, and 5 µm-thin frozen tissue sections are stained using immunohistochemistry evaluation[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Lee BI, et al. Quantification of an Antibody-Conjugated Drug in Fat Plasma by an Affinity Capture LC-MS/MS Method for a Novel Prenyl Transferase-Mediated Site-Specific Antibody-Drug Conjugate. Molecules. 2020;25(7):1515. Published 2020 Mar 26.

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