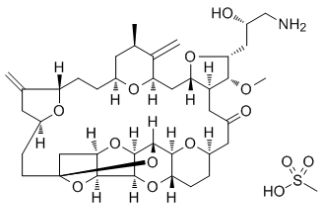
Data Sheet

Product Name:	Eribulin (mesylate)
Cat. No.:	HY-13442A
CAS No.:	441045-17-6
Molecular Formula:	$C_{41}H_{63}NO_{14}S$
Molecular Weight:	826.00
Target:	Microtubule/Tubulin
Pathway:	Cell Cycle/DNA Damage; Cytoskeleton
Solubility:	10 mM in DMSO



BIOLOGICAL ACTIVITY:

Eribulin Mesylate (E7389 Mesylate), a synthetic analogue of halichondrin B in phase III clinical trials for breast cancer, binds to tubulin and microtubules.

Target: Microtubule/Tubulin

Eribulin suppressed centromere dynamics at concentrations that arrest mitosis. At 60 nmol/L eribulin (2 x mitotic IC(50)), the relaxation rate was suppressed 21%, the time spent paused increased 67%, and dynamicity decreased 35% (but without reduction in mean centromere separation), indicating that eribulin decreased normal microtubule–dependent spindle tension at the kinetochores, preventing the signal for mitotic checkpoint passage [1]. [(3)H]eribulin binds soluble tubulin at a single site; however, this binding is complex with an overall K(d) of 46 microM, but also showing a real or apparent very high affinity (K(d) = 0.4 microM) for a subset of 25% of the tubulin. Eribulin also binds microtubules with a maximum stoichiometry of 14.7 +/– 1.3 molecules per microtubule (K(d) = 3.5 microM), strongly suggesting the presence of a relatively high–affinity binding site at microtubule ends. At 100 nM, the concentration that inhibits microtubule plus end growth by 50%, we found that one molecule of eribulin is bound per two microtubules, indicating that the binding of a single eribulin molecule at a microtubule end can potently inhibit its growth. Eribulin does not suppress dynamic instability at microtubule minus ends [2]. Eribulin's in vivo superiority derives from its ability to induce irreversible mitotic blockade, which appears related to persistent drug retention and sustained Bcl–2 phosphorylation [3].

References:

[1]. Okouneva, T., et al., Inhibition of centromere dynamics by eribulin (E7389) during mitotic metaphase. Mol Cancer Ther, 2008. 7(7): p. 2003–11.

[2]. Smith, J.A., et al., Eribulin binds at microtubule ends to a single site on tubulin to suppress dynamic instability. Biochemistry, 2010. 49(6): p. 1331–7.

[3]. Towle, M.J., et al., Eribulin induces irreversible mitotic blockade: implications of cell–based pharmacodynamics for in vivo efficacy under intermittent dosing conditions. Cancer Res, 2011. 71(2): p. 496–505.

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