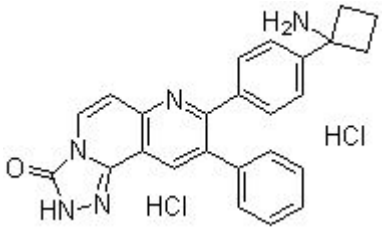
Product Introduction

MK-2206 2HCl

MK-2206 2HCl is a highly selective inhibitor of **Akt1/2/3** with **IC50** of 8 nM/12 nM/65 nM, respectively; no inhibitory activities against 250 other protein kinases observed. Phase 2.

Technical Data:

Molecular Weight (MW):	480.39	
Formula:	C25H21N5O.2HCl	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 14 mg/mL	
	Water 1 mg/mL	
	Ethanol <1 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	1032350-13-2	

Biological Activity

MK-2206 is an allosteric inhibitor and is activated by the pleckstrin homology domain. MK-2206 inhibits auto-phosphorylation of both Akt T308 and S473. MK-2206 also prevents Akt-mediated phosphorylation of downstream signaling molecules, including TSC2, PRAS40 and ribosomal S6 proteins. [1] MK-2206 inhibits Ras wild-type (WT) cell lines (A431, HCC827, and NCI-H292) more potently when compared to Ras-mutant cell lines (NCI-H358, NCI-H23, NCI-H1299, and Calu-6). MK-2206 also shows synergistic responses in combination with cytotoxic agents such as erlotinib or lapatinib in lung NCI-H460 or ovarian

A2780 tumor cells. [2] MK-2206 or siRNA-mediated Akt inhibition strongly activates autophagy in human glioma cells. However, eukaryotic elongation factor-2 (eEF-2) silencing suppresses MK-2206-induced-autophagy, with a promotion of apoptotic cell death. [3]

MK-2206 shows 60% TGI and inhibits more than 70 % of phospho-Akt1/2 (T308 and S473) in A2780 ovarian cancer xenografts at a dose of 240 mg/kg. [1] MK-2206 exhibits significant antitumor activity in NCI-H292 xenograft in combination with erlotinib or lapatinib. [2]

The first allosteric small molecule inhibitor of Akt to enter clinical development.

References

[1] Yan L, AACR Annual Meeting 2009: Abstract Number: DDT01-1.

[2] Hirai H, et al. Mol Cancer Therapy, 2010, 9(7), 1956-1967.

[3] Cheng Y, et al, Cancer Res, 2011, 71(7), 2654-2663.

[4] WO2008070016 (A2)

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