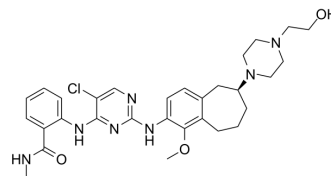


CEP-37440

Cat. No.:	HY-15841		
CAS No.:	1391712-60-9		
Molecular Formula:	C ₃₀ H ₃₈ ClN ₇ O ₃		
Molecular Weight:	580.12		
Target:	Anaplastic lymphoma kinase (ALK); FAK		
Pathway:	Protein Tyrosine Kinase/RTK		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	2 years
		-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro	DMSO : 100 mg/mL (172.38 mM; Need ultrasonic)			
		Solvent Concentration	Mass	
			1 mg	5 mg
	Preparing Stock Solutions		10 mg	
	1 mM	1.7238 mL	8.6189 mL	17.2378 mL
	5 mM	0.3448 mL	1.7238 mL	3.4476 mL
	10 mM	0.1724 mL	0.8619 mL	1.7238 mL
Please refer to the solubility information to select the appropriate solvent.				
In Vivo	<ol style="list-style-type: none"> Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline Solubility: ≥ 2.5 mg/mL (4.31 mM); Clear solution Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (4.31 mM); Clear solution Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.5 mg/mL (4.31 mM); Clear solution 			

BIOLOGICAL ACTIVITY

Description	CEP-37440 is a potent, orally active dual FAK/ALK inhibitor with IC ₅₀ values of 2.3 nM and 3.5 nM for FAK and ALK, respectively. CEP-37440 decreases the cell proliferation by blocking the autophosphorylation kinase activity of FAK1 (Tyr 397) ^{[1][2]} .
IC₅₀ & Target	IC ₅₀ : 2.3 nM (FAK) and 3.5 nM (ALK) ^[2]
In Vitro	CEP-37440 (0-3000 nM; 0-192 h) decreases the proliferation of inflammatory breast cancer (IBC) cells in a dose-dependent

manner^[1].

CEP-37440 (1000 nM; 0-120 h) decreases phospho-FAK1 (Tyr 397) and maintains its low level over time in FC-IBC02, SUM 190, and KPL4^[1].

CEP-37440 (0-3000 nM; Sup-M2 and Karpas-299 cells) induces proapoptotic caspases in a dose-dependent manner^[2].

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

Cell Viability Assay^[1]

Cell Line:	FC-IBC02, KPL4, SUM190, MDA-IBC03 and SUM149 cells
Concentration:	0, 300, 1000, 2000 and 3000 nM
Incubation Time:	0, 24, 48, 72, 96, 120, 144, 168, and 192 hours
Result:	Reduced the proliferation of three out of five IBC cell lines at low concentration. Inhibited the proliferation almost completely at 3000 nM concentration.

Western Blot Analysis^[1]

Cell Line:	FC-IBC02, SUM 190, and KPL4 cells
Concentration:	1000 nM
Incubation Time:	0, 48, 72, 96 and 120 hours
Result:	Decreased phospho-FAK1 by half in FC-IBC02, SUM190, and KPL4 cells after 48 hours.

In Vivo

CEP-37440 (3-55 mg/kg; p.o.; b.i.d and q.d., for 12 d) inhibits breast tumor growth in Sup-M2 xenograft in SCID mice^[2].

CEP-37440 (30 mg/kg; p.o; once, for 24 h) inhibits tyrosine phosphorylation in Sup-M2 xenografts mice^[2].

CEP-37440 (55 mg/kg; p.o; once, for 24 h) inhibits FAK phosphorylation in CWR22 xenografts in Nude mice^[2].

CEP-37440 (1-10 mg/kg; p.o and i.v.; CD-1 mouse, Sprague-Dawley (SD) rats) has good pharmacokinetic parameters^[2].

Pharmacokinetic parameters in CD-1 mouse and Sprague-Dawley (SD) rats^[2]

	PK parameter	CD-1 mouse	SD rat
iv	dose (mg/kg)	1	1
iv	t _{1/2} (h)	3.0	2
iv	AUC _{0-∞} (ng*h/mL)	1612	4005
iv	Vd (L/kg)	2.7	0.8
iv	CL (mL/min/kg)	10	4
po	dose (mg/kg)	10	5
po	C _{max} (ng/mL)	1533	1340

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

Animal Model:	SCID/Beige with Sup-M2 xenografts ^[2]
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Dosage:	3 mg/kg (b.i.d), 10 mg/kg (b.i.d), 30 mg/kg (b.i.d and q.d.), and 55 mg/kg (q.d.)
Administration:	Oral administration; b.i.d and q.d., for 12 days
Result:	Inhibited tumor growth in a dose-dependent manner.

Animal Model:	SCID/Beige with Sup-M2 xenografts and Nu/Nu mice female with Sup-M2 xenografts ^[2]
Dosage:	30 mg/kg
Administration:	Oral administration; once, for 24 hours
Result:	Decreased NPM-ALK phosphorylation (>85%).

Animal Model:	Nu/Nu mice female with CWR22 xenografts ^[2]
Dosage:	55 mg/kg
Administration:	Oral administration; once, for 24 hours
Result:	Inhibited FAK phosphorylation in a time-dependent manner.

REFERENCES

- [1]. Salem I, et, al. The effects of CEP-37440, an inhibitor of focal adhesion kinase, in vitro and in vivo on inflammatory breast cancer cells. *Breast Cancer Res.* 2016 Mar 24;18(1):37.
- [2]. Ott GR, et, al. Discovery of Clinical Candidate CEP-37440, a Selective Inhibitor of Focal Adhesion Kinase (FAK) and Anaplastic Lymphoma Kinase (ALK). *J Med Chem.* 2016 Aug 25;59(16):7478-96.

Caution: Product has not been fully validated for medical applications. For research use only.

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