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NVP-AEW541

Cat. No.: HY-50866

CAS No.: 475489-16-8

Molecular Formula: $C_{27}H_{29}N_5O$

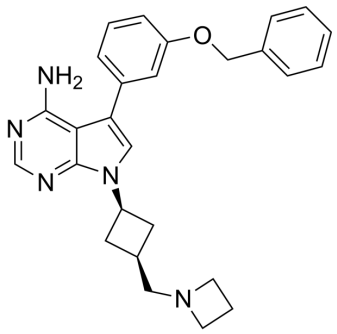
Molecular Weight: 439.55

Target: IGF-1R; Insulin Receptor; Autophagy

Pathway: Protein Tyrosine Kinase/RTK; Autophagy

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 : 50 mg/mL (113.75 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2751 mL	11.3753 mL	22.7505 mL
	5 mM	0.4550 mL	2.2751 mL	4.5501 mL
	10 mM	0.2275 mL	1.1375 mL	2.2751 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.69 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (5.69 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.69 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

NVP-AEW541 (AEW541) is an orally active inhibitor of the insulin-like growth factor 1 receptor (IGF-1R) with an IC_{50} value of 0.15 μM. NVP-AEW541 also inhibits InsR, IC_{50} with a value of 0.14 μM. NVP-AEW541 has antitumor activity[1].

IC_{50} & Target

IC50: 0.15 ±0.036 μM (IGF-IR), 0.14±0.039 μM (InsR), 0.42±0.11 μM (Flt-3), 2±0.61 μM (PDGFR), 2.4±0.38 μM (c-Src), 3.3±1.4 μM (c-Kit)[1]

In Vitro

NVP-AEW541 inhibits the in vitro kinase activity of the recombinant IGF-IR kinase domain with an IC50 value of 0.15 μM and

	to be equipotent against the recombinant InsR kinase domain. NVP-AEW541 is confirmed active toward the IGF-IR kinase (IC_{50}=86 nM) and shown to be selective at the cellular level. Indeed, NVP-AEW541 is found to be 27-fold more potent toward the native IGF-IR, as compared to the structurally related native InsR (IC_{50}=2.3 μM). NVP-AEW541 suppresses the IGF-I-mediated survival, soft agar and proliferation of MCF-7 cells with IC_{50} of 0.162 μM, 0.105 μM and 1.64 μM, respectively[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Oral administration of NVP-AEW541 (20, 30, or 50 mg/kg) results in abrogation of basal and IGF-I-induced receptor, and PKB and MAPK phosphorylation in the NWT-21 tumor xenograft[1]. NVP-AEW541 is administered by oral gavage [50 mg/kg in 0.2 mL of 25 mM L-(+)-tartaric acid] twice a day for 14 consecutive days. The control group is similarly treated with 0.2 mL carrier [25 mM L-(+)-tartaric acid] twice a day. Tumor volume and animal weight are measured thrice a week till the end of the treatment. At that time, animals are sacrificed and tumors are collected and formalin fixed for histologic and immunohistochemical analyses. In both cases, NVP-AEW541 treatment causes tumor shrinkage that reached the statistical significance (P=0.0156 and P=0.0111 for HTLA-230 and SK-N-BE2c, respectively)[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	The activities of protein kinases are assayed in the presence or absence of inhibitors by measuring the incorporation of ^{33}P from [$\gamma^{33}P$]ATP (1000 Ci/mmol) into appropriate substrates. The protein kinase assays are carried out in 96-well plates at RT under conditions described in details below andterminated by the addition of 20 μL of 125 mM EDTA. Subsequently, 30 μL (c-Abl, c-Src, IGF-1R) or 40 μL (all other kinases) of the reaction mixture are transferred onto Immobilon-PVDF pre-soaked for 5 min with methanol, rinsed with water, then soaked for 5 min with 0.5 % H_3PO_4 and mounted on vacuum manifold. After spotting all samples, vacuum is connected and each well rinsed with 200 μL 0.5 % H_3PO_4. Membranes are removed and washed 4× on a shaker with 1% H_3PO_4, once with ethanol. After drying, mounting in Packard TopCount 96- well frame, and adding of 10 μL/well of Microscint, membranes are counted. IC_{50} values are calculated by linear regression analysis of the percentage inhibition of each compound in duplicate, at four concentrations (usually 0.01, 0.1, 1, and 10 μM).One unit of protein kinase activity is defined as 1 nmole of ^{33}P transferred from [$\gamma^{33}P$]ATP to the substrate protein per minute per mg of protein at 37C[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	Between 3000 and 6000 cells/well are seeded in 96-well plates with a total media volume of 100 μL/well. Increasing concentrations of the compound are added 24 hr thereafter in quadruplicate. 72 hr later, cells are fixed by addition of 25 μL/well Glutaraldehyde (20%) and incubation for 10 min at RT. Cells are then washed 2× with 200μL/well H2O and 100μL Methylene Blue (0.05%) is added. After incubation for 10 min at RT, cells are washed 3× with 200 μL/well H_2O. 200 μL/well HCl (3%) is added, and following incubation for 30 min at RT on a plate shaker, absorbance is measured at 650 nm[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] Female Harlan athymic nude mice are used NWT-21 cells are grown in DMEM (high glucose, 4.5 g/L), 10% FCS, 1% L-glutamine, and 1% Na-pyruvate. 5×10^6 cells/animal are initially injected s.c. into the right flank of five mice. For the in vivo efficacy experiment, tumors of 500 to 800 mm^3 are excised and nonnecrotic areas are cut to fragments of 3×3×3 mm. Tumor fragments are washed in sterile PBS and one tumor fragment per animal is trans- planted s.c. into the right flank. Tumor volumes (length×width ×height×π/6) and body weights are determined three times weekly. At the first day of treatment (day 0), the therapy group (NVP-AEW541) and the control group (vehicle only) are selected by stratification (8 animals per group, average tumor volume of about 95 mm^3 per group). Animals are treated p.o. twice daily, 7 days/week either with NVP-AEW541 (20, 30, or 50 mg/kg; 10 mL/kg dissolved in 25 mM L(+)-tartaric acid, therapy group) or with 25 mM L(+)-tartaric acid (control group). Antitumor activity is expressed as T/C%(mean increase of tumor volumes of treated animals divided by the mean increase of tumor volumes of control animals multiplied by 100). The experiment is terminated when the mean tumor volume is about 1500 mm^3. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- ACS Chem Neurosci. 2021 Jul 15.
- Stem Cells Int. 06 Dec 2021.
- Endocr Relat Cancer. 2019 Feb;26(2):187-199.
- PLoS One. 2018 Feb 7;13(2):e0192214.
- Anticancer Drugs. 2023 Jul 14.

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REFERENCES

[1]. García-Echeverría C, et al. In vivo antitumor activity of NVP-AEW541-A novel, potent, and selective inhibitor of the IGF-IR kinase. Cancer Cell. 2004 Mar;5(3):231-9.

[2]. Tanno B, et al. Down-regulation of IGF-1 receptor activity by NVP-AEW541 has an antitumor effect on neuroblastoma cells in vitro and in vivo. Clin Cancer Res. 2006, 12(22), 6772-6780.

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