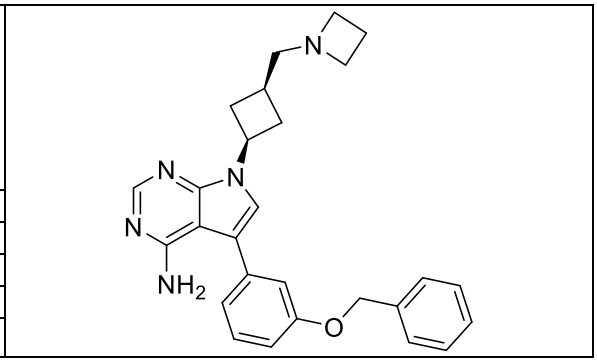
Product data sheet

MedKoo Cat#: 204210 Name: AEW-541 free base CAS#: 475489-16-8 (free base) Chemical Formula: $C_{27}H_{29}N_5O$ Exact Mass: 439.23721 Molecular Weight: 439.55	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
AEW541, also known as NVP-AEW541, is a novel, potent IGF-IR kinase inhibitor. NVP-AEW541 is capable of distinguishing between the IGF-IR (IC50 = 0.086 microM) and the closely related InsR (IC50 = 2.3 microM) in cells. NVP- AEW541 abrogates IGF-I-mediated survival and colony formation in soft agar at concentrations that are consistent with inhibition of IGF-IR autophosphorylation. Note: AEW541 has a Cis-configuration on the cyclobutane ring. Its CAS# is 475489-16-8. Many vendors and Sc-finder scholar made mistake - AEW541 was mistakenly listed as CAS#475488-34-7, the trans-isomer of AEW541. The correct structure of AEW541 can be confirmed from Joel Slade, et al (from Novartis), Org. Process Res. Dev. 2007, 11, 5, 825–835

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	50.0	113.75

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.28 mL	11.38 mL	22.75 mL
5 mM	0.46 mL	2.28 mL	4.55 mL
10 mM	0.23 mL	1.14 mL	2.28 mL
50 mM	0.05 mL	0.23 mL	0.46 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Tanno B, Mancini C, Vitali R, Mancuso M, McDowell HP, Dominici C, Raschellà G. Down-regulation of insulin-like growth factor I receptor activity by NVP-AEW541 has an antitumor effect on neuroblastoma cells in vitro and in vivo. Clin Cancer Res. 2006 Nov 15;12(22):6772-80. doi: 10.1158/1078-0432.CCR-06-1479. PMID: 17121898.
2. Scotlandi K, Manara MC, Nicoletti G, Lollini PL, Lukas S, Benini S, Croci S, Perdichizzi S, Zambelli D, Serra M, García-Echeverría C, Hofmann F, Picci P. Antitumor activity of the insulin-like growth factor-I receptor kinase inhibitor NVP-AEW541 in musculoskeletal tumors. Cancer Res. 2005 May 1;65(9):3868-76. doi: 10.1158/0008-5472.CAN-04-3192. PMID: 15867386.

In vivo study

1. Tanno B, Mancini C, Vitali R, Mancuso M, McDowell HP, Dominici C, Raschellà G. Down-regulation of insulin-like growth factor I receptor activity by NVP-AEW541 has an antitumor effect on neuroblastoma cells in vitro and in vivo. Clin Cancer Res. 2006 Nov 15;12(22):6772-80. doi: 10.1158/1078-0432.CCR-06-1479. PMID: 17121898.
2. García-Echeverría C, Pearson MA, Marti A, Meyer T, Mestan J, Zimmermann J, Gao J, Brueggen J, Capraro HG, Cozens R, Evans DB, Fabbro D, Furet P, Porta DG, Liebetanz J, Martiny-Baron G, Ruetz S, Hofmann F. 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. doi: 10.1016/s1535-6108(04)00051-0. PMID: 15050915.

7. Bioactivity

Biological target:

NVP-AEW541 (AEW541) is a potent inhibitor of IGF-1R with IC50 of 0.15 μM as well as inhibits InsR, with IC50 of 0.14 μM.

In vitro activity

To confirm the inhibitory activity of NVP-AEW541 toward IGF-IR kinase and signaling, starved TC-71 cells were treated with doses of 300 nmol/L and 1 μmol/L for 2 hours followed by stimulation with IGF-I for 5 to 30 minutes. Figure 1A shows that both IGF-IR autophosphorylation and the two major IGF-IR-related intracellular signaling pathways, MAPK and PI3K pathways, are completely inhibited by NVP-AEW541. Selective effects of NVP-AEW541 were also confirmed on IGF-I-stimulated Ewing's sarcoma proliferation. Despite the presence of the autocrine loop, Ewing's sarcoma cells maintained the ability to respond to exogenous IGF-I by moderately increasing their proliferation. Inhibitory effects of NVP-AEW541 were maintained and IGF-I could not rescue cells from growth inhibition induced by the compound (Fig. 1B). Consequently, we determined whether a daily in vitro administration of NVP-AEW541 gave a benefit in terms of growth inhibition. Figure 2B shows that similar inhibitory effects were obtained in TC-71 cells with single or a repeated treatment using NVP-AEW541. This indicates that the stable inhibition of PI3K pathway is sufficient to guarantee remarkable growth inhibitory effects of NVP-AEW541. Growth inhibitory activity of the compound was maintained for at least 72 hours after its removal (33% of growth inhibition with the dose of 300 nmol/L and 50.3% of growth inhibition with the dose of 1 μmol/L; $P < 0.05$). In conclusion, it is shown that the availability of the selective IGF-IR kinase inhibitor NVP-AEW541 may be a promising approach in the treatment of Ewing's sarcoma

Reference: Cancer Res. 2005 May 1;65(9):3868-76. https://pubmed.ncbi.nlm.nih.gov/15867386/

In vivo activity

To evaluate the antitumor activity of NVP-AEW541 in vivo, xenotransplantation experiments were carried out by injecting s.c. HTLA-230 and SK-N-BE2c cells in nude mice. Twenty million cells were injected in the flank of mice that were divided in two groups (eight mice per group). Tumors were grown until the mean volume reached ~100 mm3 (8-10 days). NVP-AEW541 was administered by oral gavage [50 mg/kg in 0.2 mL of 25 mmol/L l-(+)-tartaric acid] twice a day for 14 consecutive days. In both cases, NVP-AEW541 treatment caused tumor shrinkage (Fig. 3A and C) that reached the statistical significance ($P = 0.0156$ and $P = 0.0111$ for HTLA-230 and SK-N-BE2c, respectively). Signs of systemic toxicity (lethargy, disturbances in feeding behavior) were not observed by daily monitoring during treatment. Animal weight was not significantly different in treated and untreated animals (Fig. 3B and D). Tumors from controls were highly cellular and with a rich network of blood microvessels (Fig. 4A, B, E, and F); conversely, tumors from NVP-AEW541–treated animals showed many pyknotic cells with frequent presence of micronuclei and scant or no microvascularization (Fig. 4C, D, G, and H). A strong membrane-associated staining pattern was detectable in tumors from controls, whereas tumors from NVP-AEW541–treated animals were mostly negative (Fig. 5 , compare A, B, E, and F with C, D, G, and H). Taken together, these data indicate that NVP-AEW541 can be considered as a novel promising candidate for treatment of neuroblastoma patients.

Reference: Clin Cancer Res. 2006 Nov 15;12(22):6772-80. https://pubmed.ncbi.nlm.nih.gov/17121898/