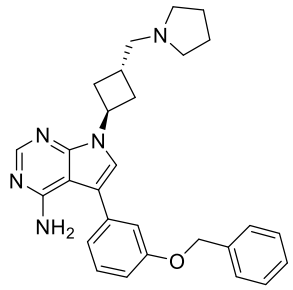
Product data sheet

MedKoo Cat#: 202042 Name: ADW742 CAS#: 475488-23-4 Chemical Formula: $C_{28}H_{31}N_5O$ Exact Mass: 453.25286 Molecular Weight: 453.57864	
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:

NVP-ADW742, also known as ADW-742 or GSK 552602A, is a novel small weight molecular inhibitor of IGF-IR with potential anticancer activity. NVP-ADW742 inhibited IGF-IR-mediated proliferation with an IC50 of 11.12 Âµmol/l. NVP-ADW742 induced early suppression of Akt, P38 and GSK-3β phosphorylation. NVP-ADW742 enhanced the chemosensitivity of Daoy to temozolomide in vitro, as a potent anti-tumor agent highly selective against IGF-IR. NVP-ADW742 was found to suppresse survival and resistance to chemotherapy in acute myeloid leukemia cells.

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	20.48	45.15
DMF	30.0	66.14
Ethanol	12.51	27.58
Ethanol:PBS (pH 7.2) (1:10)	0.09	0.20

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.20 mL	11.02 mL	22.05 mL
5 mM	0.44 mL	2.20 mL	4.41 mL
10 mM	0.22 mL	1.10 mL	2.20 mL
50 mM	0.04 mL	0.22 mL	0.44 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. Martins AS, Mackintosh C, Martín DH, Campos M, Hernández T, Ordóñez JL, de Alava E. Insulin-like growth factor I receptor pathway inhibition by ADW742, alone or in combination with imatinib, doxorubicin, or vincristine, is a novel therapeutic approach in Ewing tumor. Clin Cancer Res. 2006 Jun 1;12(11 Pt 1):3532-40. doi: 10.1158/1078-0432.CCR-05-1778. PMID: 16740780.
2. Warshamana-Greene GS, Litz J, Buchdunger E, García-Echeverría C, Hofmann F, Krystal GW. The insulin-like growth factor-I receptor kinase inhibitor, NVP-ADW742, sensitizes small cell lung cancer cell lines to the effects of chemotherapy. Clin Cancer Res. 2005 Feb 15;11(4):1563-71. doi: 10.1158/1078-0432.CCR-04-1544. PMID: 15746061.

In vivo study

1. Lahne M, Piekos SM, O'Neill J, Ackerman KM, Hyde DR. Photo-regulation of rod precursor cell proliferation. Exp Eye Res. 2019 Jan;178:148-159. doi: 10.1016/j.exer.2018.09.015. Epub 2018 Sep 27. PMID: 30267656.

2. Dent P, Han SI, Mitchell C, Studer E, Yacoub A, Grandis J, Grant S, Krystal GW, Hylemon PB. Inhibition of insulin/IGF-1 receptor signaling enhances bile acid toxicity in primary hepatocytes. Biochem Pharmacol. 2005 Nov 25;70(11):1685-96. doi: 10.1016/j.bcp.2005.08.020. Epub 2005 Oct 3. PMID: 16207485.

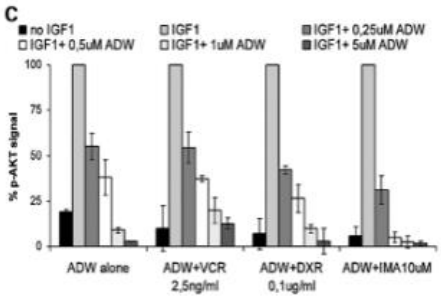
7. Bioactivity

Biological target:

NVP-ADW742 (ADW742) is an IGF-1R tyrosine kinase inhibitor with an IC50 of 0.17 μM that also inhibits insulin receptor (InsR) with an IC50 of 2.8 μM.

In vitro activity

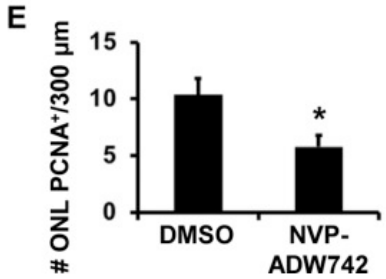
Dose-dependent blockade of basal and IGF1-induced phosphorylation was seen with ADW742 in all cell lines (IC50 of phosphorylation = 171-508 nmol/L). As shown in Fig. 1 and Supplementary Figs. S2-S4, the effects of this compound depended on the levels of IGF1R protein expression and basal phosphorylation of each cell line. Furthermore, AKT pathway activation induced by IGF1 was markedly blocked with the pretreatment with ADW742. Phospho-AKT and p-mTOR (Fig. 1C-D; Supplementary Figs. S2-4) were inhibited in a dose-dependent manner. Sensitivity to the drug showed a positive correlation with the levels of expression and basal phosphorylation of IGF1R. In contrast, MAPK42/44 remained active even when pretreated with high concentrations of ADW742, in all cell lines except A4573.



Reference: Clin Cancer Res. 2006 Jun 1;12(11 Pt 1):3532-40. https://clincancerres.aacrjournals.org/content/12/11/3532.long

In vivo activity

The IGF1-receptor inhibitor NVP-ADW742 (500 μM) or its vehicle control, DMSO (5%), were intraperitoneally injected into zebrafish every 12 h throughout the eight day dark-adaptation period. NVP-ADW742 significantly reduced the number of proliferating cells in the ONL at 8 days of dark-adaptation relative to DMSO controls (Fig. 7A–E; NVP-ADW742: 5.8 ± 1.0, n = 21; DMSO: 10.4 ± 1.4, n = 33, p = 2.5*10−6). In contrast, the low number of INL PCNA-positive cells was not affected by exposure to NVP-ADW742 (NVP-ADW742: 0.13 ± 0.07, n = 21; DMSO: 0.23 ± 0.08, n = 33, p = 0.069). Taken together, these data suggest that dark-adaptation-mediated rod precursor cell proliferation occurred in an IGF1-receptor-dependent manner.



Reference: Exp Eye Res. 2019 Jan;178:148-159. https://pubmed.ncbi.nlm.nih.gov/30267656/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.