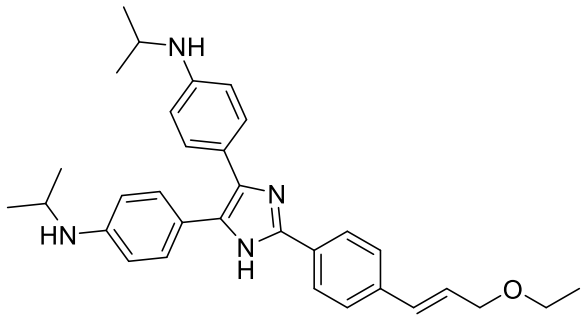
Product data sheet

MedKoo Cat#: 202055 Name: ONT-093 CAS#: 216227-54-2 Chemical Formula: $C_{32}H_{38}N_4O$ Exact Mass: 494.30456 Molecular Weight: 494.67	
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:

ONT-093, also known as OC-144-093, is an orally bioavailable P-glycoprotein pump inhibitor, for the potential reversal of multidrug resistance in patients undergoing cancer chemotherapy. ONT-093 could inhibit P-gp and reverse multidrug resistance at nM concentrations with no effect on paclitaxel pharmacokinetics. OC144-093 is the least non-specifically toxic Pgp inhibitor described to date, with an average cytostatic IC50 of >60 microM in 15 cell types. OC144-093 may represent an ideal candidate for use in enhancement of AED blood-brain barrier penetration.

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	TBD	TBD

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.02 mL	10.11 mL	20.22 mL
5 mM	0.40 mL	2.02 mL	4.04 mL
10 mM	0.20 mL	1.01 mL	2.02 mL
50 mM	0.04 mL	0.20 mL	0.40 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. Newman MJ, Rodarte JC, Benbatoul KD, Romano SJ, Zhang C, Krane S, Moran EJ, Uyeda RT, Dixon R, Guns ES, Mayer LD. Discovery and characterization of OC144-093, a novel inhibitor of P-glycoprotein-mediated multidrug resistance. Cancer Res. 2000 Jun 1;60(11):2964-72. PMID: 10850444.

In vivo study

1. Newman MJ, Rodarte JC, Benbatoul KD, Romano SJ, Zhang C, Krane S, Moran EJ, Uyeda RT, Dixon R, Guns ES, Mayer LD. Discovery and characterization of OC144-093, a novel inhibitor of P-glycoprotein-mediated multidrug resistance. Cancer Res. 2000 Jun 1;60(11):2964-72. PMID: 10850444.

7. Bioactivity

Biological target:

ONT-093, also known as OC-144-093, is a P-glycoprotein pump inhibitor with an average cytostatic IC50 of >60 microM in 15 cell types.

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In vitro activity

OC144-093 was able to reverse resistance to all classes of P-gp substrates in a wide variety of tumor cell types with EC50s in the low nm range (Table 1). Complete reversal of MDR was typically seen with OC144-093 doses between 0.25 and 1.0 μm. Examples with cells expressing extremely high levels of P-gp as a result of drug selection (CEM/VLB1000), moderate levels of P-gp from gene transduction (MDA/LCC6MDR1), and low (intrinsic) levels of P-gp (HCT-15) are illustrated in detail in Fig. 2 . OC144-093 had no effect on doxorubicin or paclitaxel IC50s in non-P-gp-expressing CCRF-CEM and MDA/LCC6 cells, respectively, demonstrating the specificity of this compound for P-gp. OC144-093 retained full MDR reversal potency after incubation in human plasma, suggesting that protein binding-mediated inactivation will not be a problem in humans (data not shown). OC144-093 was able to reverse paclitaxel resistance in P-gp-expressing MCF-7/ADR cells by almost four orders of magnitude. OC144-093 had no effect on paclitaxel or etoposide IC50s in non-P-gp-expressing MCF-7 cells, further supporting the specificity of the compound for P-gp (data not shown). The HCT-15 human colon carcinoma cell line was derived from a patient not previously exposed to antitumor agents. OC144-093 was able to significantly reverse resistance to paclitaxel in this cell line in vitro (Fig. 2C).

Reference: Cancer Res. 2000 Jun 1;60(11):2964-72. https://pubmed.ncbi.nlm.nih.gov/10850444/

In vivo activity

A standard i.p. P338 murine leukemia model of MDR was chosen for initial in vivo studies. OC144-093 (20 mg/kg) was found to almost completely reverse resistance to doxorubicin in this model. A dose-response for MDR reversal was observed at the lower doses (Table 4). On the bases of animal weight and mortality, no significant or reproducible enhancement of toxicity was observed when OC144-093 was combined with doxorubicin at the concentrations indicated. OC144-093 had no significant effect, by itself, on the survival of mice implanted with wild-type or MDR P388 ascites tumors (wild-type data not shown). In addition, OC144-093 did not enhance the life span of doxorubicin-treated mice implanted with wild-type P388 ascites tumors (Table 4) . The growth delay produced by paclitaxel and OC144-093 in the MDA/LCC6MDR1 xenografts was comparable with the growth delay produced by paclitaxel alone in MDA/LCC6 xenografts, suggesting complete reversal of MDR by OC144-093 (data not shown).

Reference: Cancer Res. 2000 Jun 1;60(11):2964-72. https://pubmed.ncbi.nlm.nih.gov/10850444/