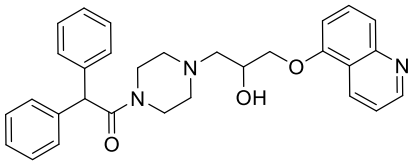
Product data sheet

MedKoo Cat#: 201065 Name: Dofequidar CAS#: 129716-58-1 (free base) Chemical Formula: $C_{30}H_{31}N_3O_3$ Exact Mass: 481.23654 Molecular Weight: 481.59	
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:

Dofequidar, also known as MS-209, is a quinolone-derived sphingomyelin synthase inhibitor that blocks P-glycoprotein and multidrug resistance-associated protein-1, is under development by Schering for the potential treatment of multidrug resistant tumors. Dofequidar was found to sensitizes cancer stem-like side population cells to chemotherapeutic drugs by inhibiting ABCG2/BCRP-mediated drug export.

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
TBD	TBD	TBD

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.08 mL	10.38 mL	20.76 mL
5 mM	0.42 mL	2.08 mL	4.15 mL
10 mM	0.21 mL	1.04 mL	2.08 mL
50 mM	0.04 mL	0.21 mL	0.42 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. Katayama R, Koike S, Sato S, Sugimoto Y, Tsuruo T, Fujita N. Dofequidar fumarate sensitizes cancer stem-like side population cells to chemotherapeutic drugs by inhibiting ABCG2/BCRP-mediated drug export. Cancer Sci. 2009 Nov;100(11):2060-8. doi: 10.1111/j.1349-7006.2009.01288.x. Epub 2009 Jul 17. PMID: 19673889.

In vivo study

1. Katayama R, Koike S, Sato S, Sugimoto Y, Tsuruo T, Fujita N. Dofequidar fumarate sensitizes cancer stem-like side population cells to chemotherapeutic drugs by inhibiting ABCG2/BCRP-mediated drug export. Cancer Sci. 2009 Nov;100(11):2060-8. doi: 10.1111/j.1349-7006.2009.01288.x. Epub 2009 Jul 17. PMID: 19673889.

7. Bioactivity

Biological target:

Dofequidar(MS-209) is a novel quinoline compound, which can reverse P-glycoprotein (P-gp)-mediated MDR.

In vitro activity

Product data sheet

Because dofequidar could reduce the cell number in the SP fraction that highly expressed ABCG2/BCRP (Figs 3,4), it was hypothesized that dofequidar had the ability to inhibit ABCG2/BCRP in addition to the previously reported ABCB1/P-gp and ABCC1/MRP1. Parental K562 cells or K562 stable transfectants were stained with Hoechst33342 in the presence or absence of ABC-T inhibitors. Dofequidar but not verapamil could increase the intracellular Hoechst33342 concentration in K562/BCRP cells dose dependently (Fig. S1B). Similar results were obtained in KB/BCRP cells (data not shown). To confirm the result, this study carried out an in vitro vesicle transport assay. Membrane vesicles from control or ABCG2/BCRP-overexpressing insect cells were incubated with [^{3}H]MTX in the presence of ATP or AMP. The ATP-dependent uptake of [^{3}H]MTX was observed in ABCG2/BCRP-overexpressing membrane vesicles but not in control vesicles (Fig. 4A). FTC (Fumitremorgin C) and dofequidar, but not verapamil, inhibited [^{3}H]MTX uptake dose dependently (Fig. 5A). These results suggest that dofequidar had the ability to inhibit ABCG2/BCRP in addition to the previously reported ABCB1/P-gp and ABCC1/MRP1.

Reference: Cancer Sci. 2009 Nov;100(11):2060-8. https://onlinelibrary.wiley.com/doi/full/10.1111/j.1349-7006.2009.01288.x

In vivo activity

FTC is not suitable for clinical studies because of its severe toxicity, but it strongly and specifically inhibits ABCG2/BCRP. On the other hand, dofequidar exhibits low toxicity and has already been approved for clinical trials. To overcome the chemoresistance of cancer stem-like SP cells in vivo, this study evaluated the antitumor activity of CPT-11 plus dofequidar in a clinically relevant model. HeLa-derived SP and NSP cells were transplanted into nude mice, and the xenografted tumors were treated with CPT-11 with or without dofequidar. Dofequidar (200 mg/kg) was orally administrated 30 min before CPT-11 (67 mg/kg) injection. Although xenografted HeLa SP cells showed resistance to CPT-11, co-treatment of the mice with dofequidar drastically decreased the tumor volume (Fig. 6B, left panel), like that seen in CPT-11-treated or CPT-11 plus dofequidar-treated NSP-bearing mice (Fig. 6B, right panel). Dofequidar alone had almost no effect on SP- or NSP-derived tumor growth in vivo. To assess the toxicity, the study measured the bodyweight of the tumor-bearing mice. The mice seemed to be healthy (Fig. 6C), and the change in bodyweight was very small (data not shown). Thus CPT-11 plus dofequidar therapy appeared to have good therapeutic efficacy in vivo by sensitizing cancer stem-like cells to anticancer drugs.

Reference: Cancer Sci. 2009 Nov;100(11):2060-8. https://onlinelibrary.wiley.com/doi/full/10.1111/j.1349-7006.2009.01288.x