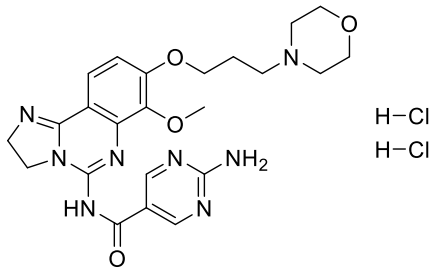
Product data sheet

MedKoo Cat#: 206945 Name: Copanlisib HCl CAS#: 1402152-13-9 (HCl) Chemical Formula: $C_{23}H_{30}Cl_2N_8O_4$ Molecular Weight: 553.445	
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:

Copanlisib also known as BAY 80-6946, is a potent phosphoinositide 3-kinase (PI3K) inhibitor. Copanlisib inhibits the activation of the PI3K signaling pathway, which may result in inhibition of tumor cell growth and survival in susceptible tumor cell populations. Activation of the PI3K signaling pathway is frequently associated with tumorigenesis and dysregulated PI3K signaling may contribute to tumor resistance to a variety of antineoplastic agents. Copanlisib was approved for the treatment of adult patients experiencing relapsed follicular lymphoma who have received at least two prior systemic therapies.

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	1	2.08
Water	0.67	1.39

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.81 mL	9.03 mL	18.07 mL
5 mM	0.36 mL	1.81 mL	3.61 mL
10 mM	0.18 mL	0.90 mL	1.81 mL
50 mM	0.04 mL	0.18 mL	0.36 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. Liu N, Rowley BR, Bull CO, Schneider C, Haegebarth A, Schatz CA, Fracasso PR, Wilkie DP, Hentemann M, Wilhelm SM, Scott WJ, Mumberg D, Ziegelbauer K. BAY 80-6946 is a highly selective intravenous PI3K inhibitor with potent p110α and p110δ activities in tumor cell lines and xenograft models. Mol Cancer Ther. 2013 Nov;12(11):2319-30. doi: 10.1158/1535-7163.MCT-12-0993-T. Epub 2013 Oct 29. PMID: 24170767.

2. Schneider P, Schön M, Pletz N, Seitz CS, Liu N, Ziegelbauer K, Zachmann K, Emmert S, Schön MP. The novel PI3 kinase inhibitor, BAY 80-6946, impairs melanoma growth in vivo and in vitro. Exp Dermatol. 2014 Aug;23(8):579-84. doi: 10.1111/exd.12470. PMID: 24942196.

In vivo study

1. Liu N, Rowley BR, Bull CO, Schneider C, Haegebarth A, Schatz CA, Fracasso PR, Wilkie DP, Hentemann M, Wilhelm SM, Scott WJ, Mumberg D, Ziegelbauer K. BAY 80-6946 is a highly selective intravenous PI3K inhibitor with potent p110α and p110δ activities in tumor cell lines and xenograft models. Mol Cancer Ther. 2013 Nov;12(11):2319-30. doi: 10.1158/1535-7163.MCT-12-0993-T. Epub 2013 Oct 29. PMID: 24170767.

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2. Schneider P, Schön M, Pletz N, Seitz CS, Liu N, Ziegelbauer K, Zachmann K, Emmert S, Schön MP. The novel PI3 kinase inhibitor, BAY 80-6946, impairs melanoma growth in vivo and in vitro. Exp Dermatol. 2014 Aug;23(8):579-84. doi: 10.1111/exd.12470. PMID: 24942196.

7. Bioactivity

Biological target:

Copanlisib (BAY 80-6946) is a potent, selective and ATP-competitive pan-class I PI3K inhibitor, with IC50s of 0.5 nM, 0.7 nM, 3.7 nM and 6.4 nM for PI3Kα, PI3Kδ, PI3Kβ and PI3Kγ, respectively.

In vitro activity

BAY 80-6946 potently inhibited the catalytic activity of the class I PI3Kα, β, γ, and δ isoforms with IC50 values of 0.5, 3.7, 6.4, and 0.7 nmol/L, respectively. It showed significantly weaker activity against mTOR with an IC50 of 45 nmol/L. In contrast, 1 μmol/L BAY 80-6946 did not inhibit PI4K-II, PIP4-5K, PIP5-4K, or an additional 220 kinases in the Millipore kinase panel (inhibition <30%), indicating that BAY 80-6946 is a specific PI3K inhibitor with more than 2,000-fold selectivity against other lipid and protein kinases, except for mTOR. To further evaluate the selectivity of BAY 80-6946 against PI3K versus mTOR kinase, rat ELT3 cells, which exhibit a PI3K-independent activation of mTORC1 due to TCS2 deficiency, were used. Complete inhibition of PI3K-mediated AKT phosphorylation was clearly shown at a concentration of 5 nmol/L (Fig. 1B), whereas BAY 80-6946 showed only a minor reduction of PI3K-independent mTORC1-mediated phosphorylation of S70S6K levels and no effect at all on p-4E-BP1 at a concentration of 500 nmol/L (Fig. 1C).

Reference: Mol Cancer Ther. 2013 Nov;12(11):2319-30. http://mct.aacrjournals.org/cgi/pmidlookup?view=long&pmid=24170767

In vivo activity

BAY 80-6946 is highly efficacious in rat and mouse tumor xenograft models following intravenous administration. BAY 80-6946 was well tolerated at all doses and schedules tested in the studies described here without producing any lethality. The maximum-tolerated dose (MTD) in rats was defined as 6 mg/kg. At the MTD, a maximum mean body weight loss of 6% to 10% occurred during the first few days of dosing and then consistently returned to the normal range by the end of the dosing period. The MTD in mice was more than 14 mg/kg with a every second day dosing schedule. BAY 80-6946 was highly efficacious in a variety of human tumor xenograft models derived from different tumor indications that exhibit an activated PI3K pathway. The drug displayed robust antitumor activity in the rat KPL4 tumor xenograft model, which is an estrogen-independent HER2-positive breast carcinoma that carries a somatic PIK3CA mutation. BAY 80-6946 was administered at 0.5 to 6 mg/kg i.v. every second day for a total of five doses starting on day 14, following tumor cell implantation. On day 25, 3 days after the last dose, TGI rates of 77%, 84%, 99%, and 100% were observed with BAY 80-6946 at doses of 0.5, 1, 3, and 6 mg/kg, respectively (Fig. 5A). Complete tumor regression was shown in 10 of 10 rats in the 3 and 6 mg/kg groups, and all rats remained tumor free at the termination of the study on day 73. Tumor growth delays more than 25 days were observed in the 0.5 and 1 mg/kg dose groups.

Reference: Mol Cancer Ther. 2013 Nov;12(11):2319-30. http://mct.aacrjournals.org/cgi/pmidlookup?view=long&pmid=24170767