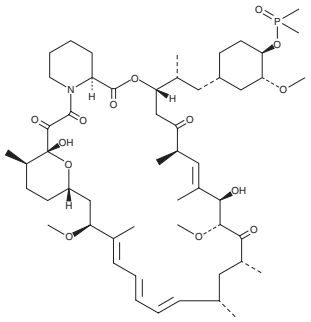
PRODUCT INFORMATION

MK-8669

Item No. 10543



CAS Registry No.:	572924-54-0
Formal Name:	42-(dimethylphosphinate)rapamycin
Synonyms:	AP23573, Deforolimus, Ridaforolimus
MF:	$C_{53}H_{84}NO_{14}P$
FW:	990.2
Purity:	≥95%
UV/Vis.:	λ_{max}: 204, 267, 277, 289 nm
Supplied as:	A crystalline solid
Storage:	-20°C
Stability:	≥4 years

Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

MK-8669 is supplied as a crystalline solid. A stock solution may be made by dissolving the MK-8669 in the solvent of choice. MK-8669 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF), which should be purged with an inert gas. The solubility of MK-8669 in these solvents is approximately 5, 20, and 30 mg/ml, respectively.

MK-8669 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, MK-8669 should first be dissolved in DMF and then diluted with the aqueous buffer of choice. MK-8669 has a solubility of approximately 0.33 mg/ml in a 1:2 solution of DMF:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

MK-8669 is a rapamycin analog that selectively inhibits mTOR (IC_{50} = 0.2 nM). Like rapamycin, MK-8669 binds FKBP12 to form a complex that associates with the FKBP-rapamycin binding domain on mTOR and allosterically inhibits mTORC1 kinase activity.[1] MK-8669 is more water soluble than rapamycin and is amenable to oral or intravenous administration. Formulations containing rapalogs, including MK-8669, have promise against a subset of cancers, including advanced kidney cancer.[1] MK-8669 is also being examined for effectiveness against cancers when used in combination with other chemotherapeutic compounds.[2-4]

References

1. Benjamin, D., Colombi, M., Moroni, C., *et al.* Rapamycin passes the torch: A new generation of mTOR inhibitors. *Nat. Rev. Drug Discov.* **10(11)**, 868-880 (2011).
2. Becker, M.A., Hou, X., Tienchaianada, P., *et al.* Ridaforolimus (MK-8669) synergizes with dalotuzumab (MK-0646) in hormone-sensitive breast cancer. *BMC Cancer* **16(1)**, 814 (2016).
3. Hernandez, S.F., Chisholm, S., Borger, D., *et al.* Ridaforolimus improves the anti-tumor activity of dual HER2 blockade in uterine serous carcinoma *in vivo* models with HER2 gene amplification and PIK3CA mutation. *Gynecol. Oncol.* **141(3)**, 570-579 (2016).
4. Lamhamedi-Cherradi, S.-E., Menegaz, B.A., Ramamoorthy, V., *et al.* IGF-1R and mTOR blockade: Novel resistance mechanisms and synergistic drug combinations for Ewing sarcoma. *J. Natl. Cancer Inst.* **108(12)**, (2016).

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