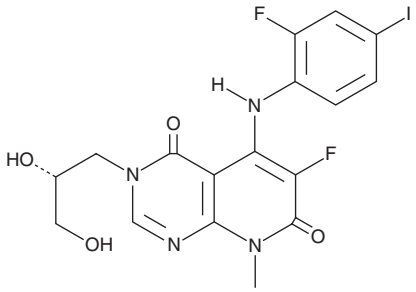
PRODUCT INFORMATION

TAK-733

Item No. 16998

CAS Registry No.:	1035555-63-5
Formal Name:	3-[(2R)-2,3-dihydroxypropyl]-6-fluoro-5-[(2-fluoro-4-iodophenyl)amino]-8-methyl-pyrido[2,3-d]pyrimidine-4,7(3H,8H)-dione
MF:	$C_{17}H_{15}F_2IN_4O_4$
FW:	504.2
Purity:	≥98%
UV/Vis.:	λ_{max}: 239, 293 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

TAK-733 is supplied as a crystalline solid. A stock solution may be made by dissolving the TAK-733 in the solvent of choice. TAK-733 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF), which should be purged with an inert gas. The solubility of TAK-733 in ethanol is approximately 0.25 mg/ml and approximately 30 mg/ml in DMSO and DMF.

TAK-733 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, TAK-733 should first be dissolved in DMSO and then diluted with the aqueous buffer of choice. TAK-733 has a solubility of approximately 0.1 mg/ml in a 1:9 solution of DMSO:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

TAK-733 is an inhibitor of MEK1 (IC_{50} = 3.2 nM), a MAP kinase in the Raf/MEK/ERK pathway that plays a major role in the regulation of cellular growth, differentiation, and proliferation.[1,2] It is selective for MEK1 over a panel of 18 kinases, receptors, and ion channels up to a concentration of 10 µM. TAK-733 inhibits ERK phosphorylation *in vitro* (EC_{50} = 1.9 nM). It also inhibits proliferation of A375 and COLO 205 cells (EC_{50}s = 3.1 and 2.1 nM, respectively) and 14 cutaneous melanoma cell lines (IC_{50}s = <1-10 nM), particularly those with $B\text{-}RAF^{V600E}$ mutations.[1,3] TAK-733 has antitumor activity in mouse xenograft models using a variety of cancer types.[1]

References

1. Dong, Q., Dougan, D.R., Gong, X., *et al*. Discovery of TAK-733, a potent and selective MEK allosteric site inhibitor for the treatment of cancer. *Bioorg. Med. Chem. Lett.* **21(5)**, 1315-1319 (2011).
2. Cowan, K.J. and Storey, K.B. Mitogen-activated protein kinases: New signaling pathways functioning in cellular responses to environmental stress. *J. Exp. Biol.* **206(Pt 7)**, 1107-1115 (2003).
3. von Euw, E., Atefi, M., Attar, N., *et al*. Antitumor effects of the investigational selective MEK inhibitor TAK733 against cutaneous and uveal melanoma cell lines. *Mol. Cancer* **11**, 22 (2012).

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