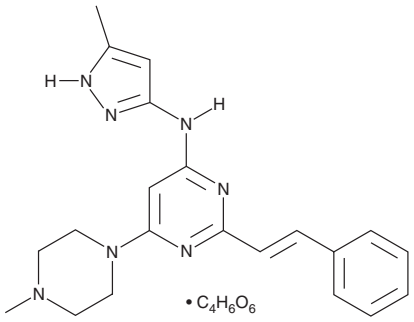
PRODUCT INFORMATION

ENMD-2076

Item No. 22956

CAS Registry No.:	1453868-32-0
Formal Name:	6-(4-methyl-1-piperazinyl)-N-(5-methyl-1H-pyrazol-3-yl)-2-[(1E)-2-phenylethenyl]-4-pyrimidinamine, 2R,3R-dihydroxybutanedioate
MF:	$C_{21}H_{25}N_7 \bullet C_4H_6O_6$
FW:	525.6
Purity:	≥98%
UV/Vis.:	λ_{max}: 203, 269 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

ENMD-2076 is supplied as a crystalline solid. A stock solution may be made by dissolving the ENMD-2076 in the solvent of choice, which should be purged with an inert gas. ENMD-2076 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF). The solubility of ENMD-2076 in ethanol is approximately 5 mg/ml and approximately 20 mg/ml in DMSO and DMF.

ENMD-2076 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, ENMD-2076 should first be dissolved in DMSO and then diluted with the aqueous buffer of choice. ENMD-2076 has a solubility of approximately 0.5 mg/ml in a 1:1 solution of DMSO:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

ENMD-2076 is a multi-kinase inhibitor that inhibits FMS-related tyrosine kinase 3 (FLT3), RET, and Aurora A kinase with IC_{50} values of 1.86, 10.4, and 14 nM, respectively.[1] It inhibits additional kinases involved in angiogenesis such as VEGFR3, PDGFRα, and FGFR2, among others, with IC_{50} values of less than 100 nM. It inhibits proliferation of several human triple-negative breast cancer (TNBC) cell lines with IC_{50} values of less than 1 µM, halts the cell cycle at the G_2 phase, and induces apoptosis.[2] Oral administration of ENMD-2076 (200 mg/kg), reduces proliferation, enhances p53- and p73-mediated cancer cell apoptosis and senescence, and inhibits growth of sensitive primary tumors in a TNBC mouse xenograft model.[3] It also decreases tumor vascular permeability and perfusion and inhibits tumor growth in human TNBC and colorectal cancer mouse xenograft models when administered orally at a dose of 100 mg/kg.[2,4]

References

1. Fletcher, G.C., Brokx, R.D., Denny, T.A., *et al.* ENMD-2076 is an orally active kinase inhibitor with antiangiogenic and antiproliferative mechanisms of action. *Mol. Cancer Ther.* **10(1)**, 126-137 (2011).
2. Diamond, J.R., Eckhardt, S.G., Tan, A.C., *et al.* Predictive biomarkers of sensitivity to the aurora and angiogenic kinase inhibitor ENMD-2076 in preclinical breast cancer models. *Clin. Cancer Res.* **19(1)**, 291-303 (2013).
3. Ionkina, A.A., Tentler, J.J., Kim, J., *et al.* Efficacy and molecular mechanisms of differentiated response to the aurora and angiogenic kinase inhibitor ENMD-2076 in preclinical models of p53-mutated triple-negative breast cancer. *Front. Oncol.* **7(94)**, (2017).
4. Tentler, J.J., Bradshaw-Pierce, E.L., Serkova, N.J., *et al.* Assessment of the *in vivo* antitumor effects of ENMD-2076, a novel multitargeted kinase inhibitor, against primary and cell line-derived human colorectal cancer xenograft models. *Clin. Cancer Res.* **16(11)**, 2989-2998 (2010).

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