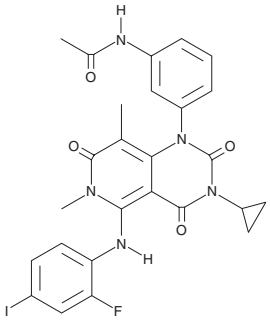
PRODUCT INFORMATION

Trametinib

Item No. 16292

CAS Registry No.:	871700-17-3
Formal Name:	N-[3-[3-cyclopropyl-5-[(2-fluoro-4-iodophenyl)amino]-3,4,6,7-tetrahydro-6,8-dimethyl-2,4,7-trioxopyrido[4,3-d]pyrimidin-1(2H)-yl]phenyl]-acetamide
Synonyms:	GSK1120212, JTP-74057
MF:	$C_{26}H_{23}FIN_5O_4$
FW:	615.4
Purity:	≥95%
UV/Vis.:	λ_{max}: 250, 330 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

Trametinib is supplied as a crystalline solid. A stock solution may be made by dissolving the trametinib in the solvent of choice. Trametinib is soluble in organic solvents such as DMSO and dimethyl formamide, which should be purged with an inert gas. The solubility of trametinib in these solvents is approximately 3 and 2 mg/ml, respectively.

Trametinib is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, trametinib should first be dissolved in DMSO and then diluted with the aqueous buffer of choice. Trametinib has a solubility of approximately 0.3 mg/ml in a 1:2 solution of DMSO:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

Trametinib is an inhibitor of MEK1 and -2.[1] It inhibits B-RAF- and C-RAF-induced phosphorylation of MEK1 (IC_{50}s = 3.4 and 1.8 nM, respectively) and MEK2 (IC_{50}s = 1.6 and 0.92 nM, respectively). Trametinib inhibits the growth of two human colorectal cancer cell lines expressing mutant B-RAF (IC_{50}s = 0.48 and 0.52 nM) and seven cell lines expressing mutant K-Ras (IC_{50}s = 2.2-174 nM) but does not inhibit the growth of wild-type COLO 320DM cells expressing both B-RAF and K-Ras (IC_{50} = >10,000 nM). It reduces tumor growth in HT-29 and COLO 205 mouse xenograft models when used at doses of 0.3 and 1 mg/kg per day. Trametinib (0.03 and 0.1 mg/kg per day) also decreases *M. tuberculosis*-induced increases in hind paw volume in a rat model of arthritis.[2] Formulations containing trametinib, in combination with dabrafenib, have been used in the treatment of metastatic mutant B-RAF^{V600E} melanoma.

References

1. Yamaguchi, T., Kakefuda, R., Tajima, N., *et al.* Antitumor activities of JTP-74057 (GSK1120212), a novel MEK1/2 inhibitor, on colorectal cancer cell lines *in vitro* and *in vivo*. *Int. J. Oncol.* **39(1)**, 23-31 (2011).
2. Yamaguchi, T., Kakefuda, R., Tanimoto, A., *et al.* Suppressive effect of an orally active MEK1/2 inhibitor in two different animal models for rheumatoid arthritis: A comparison with leflunomide. *Inflamm. Res.* **61(5)**, 445-454 (2012).

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