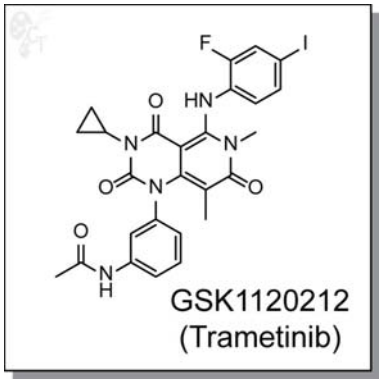
Product Specification Sheet

Product Name: GSK1120212 (Trametinib)

Catalog Number: C4112



Technical information:

Chemical Formula:	$C_{26}H_{23}FIN_5O_4$
CAS #:	871700-17-3
Molecular Weight:	615.39
Purity:	> 98%
Appearance:	White solid
Solubility:	Soluble in DMSO up to 10 mM
Chemical Name:	N-(3-(3-cyclopropyl-5-(2-fluoro-4-iodophenylamino)-6,8-dimethyl-2,4,7-trioxo-3,4,6,7-tetrahydropyrido[4,3-d]pyrimidin-1(2H)-yl)phenyl)acetamide
Storage:	Store solid powder at 4°C desiccated; Store DMSO solution at -20°C.
Shelf Life:	In the unopened package, powder is stable for 1 year and DMSO solution is stable for 6 months under proper storage condition.

Handling:

- To make 10 mM stock solution, add 0.162mL of DMSO for each mg of GSK1120212 (Trametinib)
- For DMSO solution, briefly spin the vial at 500 rpm in a 50 mL conical tube to ensure maximum sample recovery.

Biological Activity:

Trametinib (GSK1120212) is an orally-available, tetrahydropyridopyrimidine-based, allosteric inhibitor of MEK1 and MEK2, with an IC50 of 1.6 and 3.4 nM when using B-Raf as its activator. [1] It is highly selective over broad inhibitory panel of 98 kinases at 10 uM. In vitro, Trametinib strongly inhibits human colorectal cancer cell lines known to have a constitutively active B-Raf or Ras mutation; in particular, IC50 inhibition values of HT-29, COLO205, HCT116, LS-174T, and SW620 are 0.48, 0.52, 5.7, 4.1, and 2.3 nM, respectively. [1]

Trametinib prevents Raf-dependent MEK phosphorylation (S217 for MEK1), resulting in prolonged p-Erk1/2 inhibition. [2] In a broad panel of cancer cell lines, Trametinib was shown to inhibit the MEK1/2-dependent activating dual phosphorylation of ERK1/2 on both T202 and Y204.

Trametinib has been shown to work in combination with other B-Raf inhibitors, overcoming resistant lines mediated by NRAS or MEK mutations. [3]

Reference:

1. Yamaguchi 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. 2011, 39(1), 23-31. Pubmed ID: 21523318
2. Gilmartin et al., GSK1120212 (JTP-74057) is an inhibitor of MEK activity and activation with favorable pharmacokinetic properties for sustained in vivo pathway inhibition. Clin. Cancer Res. 2011, 17, 989-1000. Pubmed ID: 21245089
3. Greger et al., Combinations of BRAF, MEK, and PI3K/mTOR inhibitors overcome acquired resistance to the BRAF inhibitor GSK2118436 dabrafenib, mediated by NRAS or MEK mutations. Mol. Cancer Ther. 2012, 11(4), 909-920. Pubmed ID: 22389471

To reorder: http://www.cellagentech.com/GSK1120212-Trametinib/
For Technical Support: technical@cellagentech.com

Chemicals are sold for research use only, not for clinical or diagnostic use.