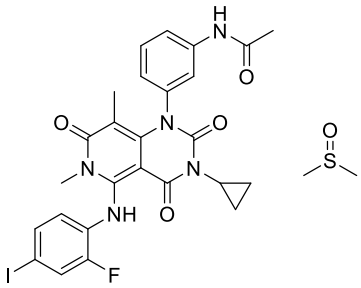
Product data sheet

MedKoo Cat#: 123211 Name: Trametinib DMSO solvate CAS#: 1187431-43-1 Chemical Formula: $C_{28}H_{29}FIN_5O_5S$ Molecular Weight: 693.09	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

Trametinib DMSO solvate is a solvated form of trametinib at 1:1 molar ratio of trametinib to dimethyl sulfoxide. Trametinib, also known as GSK1120212, GSK212 or JTP74057, is an approved and new targeted drug for the treatment of melanoma. It is a powerful and selective MEK1/MEK2 inhibitor which can effectively prevent cancer cell proliferating and can induce cell apoptosis, and increase the life of patients.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	59.5	85.85

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.44 mL	7.21 mL	14.43 mL
5 mM	0.29 mL	1.44 mL	2.89 mL
10 mM	0.14 mL	0.72 mL	1.44 mL
50 mM	0.03 mL	0.14 mL	0.29 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Itamura H, Shindo T, Tawara I, Kubota Y, Kariya R, Okada S, Komanduri KV, Kimura S. The MEK inhibitor trametinib separates murine graft-versus-host disease from graft-versus-tumor effects. JCI Insight. 2016 Jul 7;1(10):e86331. doi: 10.1172/jci.insight.86331. PMID: 27699218; PMCID: PMC5033881.
2. Bridgeman VL, Wan E, Foo S, Nathan MR, Welti JC, Frentzas S, Vermeulen PB, Preece N, Springer CJ, Powles T, Nathan PD, Larkin J, Gore M, Vasudev NS, Reynolds AR. Preclinical Evidence That Trametinib Enhances the Response to Antiangiogenic Tyrosine Kinase Inhibitors in Renal Cell Carcinoma. Mol Cancer Ther. 2016 Jan;15(1):172-83. doi: 10.1158/1535-7163.MCT-15-0170. Epub 2015 Oct 20. PMID: 26487278.

In vivo study

1. Tada S, Anazawa T, Shindo T, Yamane K, Inoguchi K, Fujimoto N, Nagai K, Masui T, Okajima H, Takaori K, Sumi S, Uemoto S. The MEK Inhibitor Trametinib Suppresses Major Histocompatibility Antigen-mismatched Rejection Following Pancreatic Islet Transplantation. Transplant Direct. 2020 Aug 12;6(9):e591. doi: 10.1097/TXD.0000000000001045. PMID: 32851124; PMCID: PMC7423917.
2. Bridgeman VL, Wan E, Foo S, Nathan MR, Welti JC, Frentzas S, Vermeulen PB, Preece N, Springer CJ, Powles T, Nathan PD, Larkin J, Gore M, Vasudev NS, Reynolds AR. Preclinical Evidence That Trametinib Enhances the Response to Antiangiogenic

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Tyrosine Kinase Inhibitors in Renal Cell Carcinoma. Mol Cancer Ther. 2016 Jan;15(1):172-83. doi: 10.1158/1535-7163.MCT-15-0170. Epub 2015 Oct 20. PMID: 26487278.

7. Bioactivity

Biological target:

Trametinib (GSK1120212; JTP-74057) is an MEK inhibitor that inhibits MEK1 and MEK2 with IC50s of about 2 nM.

In vitro activity

Interestingly, several IAV (Influenza A virus)-induced cytokines were reduced on mRNA level in presence of Trametinib (Fig. 4A and B). The expression of IFNβ and the interferon stimulated gene (ISG) MxA was only found to be reduced by Trametinib in infected cells (Fig. 4A), but not strongly affected in vRNA-transfected cells (Fig. 4C). The results indicate that the cellular IFN response is not directly limited by Trametinib. Rather it seems to be primarily indirectly affected by reduced viral replication than being directly caused by deregulation of the Raf/MEK/ERK signaling cascade. Indeed, expression of IFNβ and MxA are not yet described to be directly regulated by the Raf/MEK/ERK signaling cascade. Considering Trametinib as antiviral drug it is beneficial that Trametinib does not directly alter the IFN response which is an important arm of cellular antiviral defense. A clearly decreased induction by Trametinib was also detectable for IL6, CCL5 and CXCL10 mRNA expression, which were induced by infection with PR8M/H1N1 (Fig. 4B).

Reference: Mol Cancer Ther. 2016 Jan;15(1):172-83. https://pubmed.ncbi.nlm.nih.gov/29990517/

In vivo activity

This study examined the mechanism by which trametinib impacts T-cell subpopulations after islet transplantation. T-cell subpopulations isolated from the liver and spleen of recipient mice on day 7, which were treated with vehicle or with 0.1 or 0.3 mg/kg trametinib, were analyzed by flow cytometry (n = 3/group). The ratio of $CD8^+$ T cells to $CD4^+$ T cells in the liver of trametinib-treated mice tended to be lower than that in the vehicle-treated group (Figure 4A; 1-way ANOVA; $P = 0.26$), indicating that trametinib suppresses infiltration of the liver by $CD8^+$ T cells. Among the different $CD4^+$ T-cell subpopulations, trametinib increased the percentage of naive T cells ($CD62L^+CD44–$) in the liver in a dose-dependent manner; it also reduced the percentage of effector memory T cells ($CD62L\text{-}CD44^+$) in the liver and spleen (Figure 4B; 1-way ANOVA; all $P < 0.05$). By contrast, trametinib had no effect on $CD8^+$ T-cell subpopulations in the liver or spleen (Figure 4C). These results suggest that (at least in vivo) trametinib mainly suppresses functional differentiation of $CD4^+$ naive T cells.

Reference: Transplant Direct. 2020 Sep; 6(9): e591. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7423917/