# Trametiglue

**Cat. No.:** HY-153181

**CAS No.:** 2666940-97-0

**Molecular Formula:** $C_{25}H_{24}FIN_6O_5S$

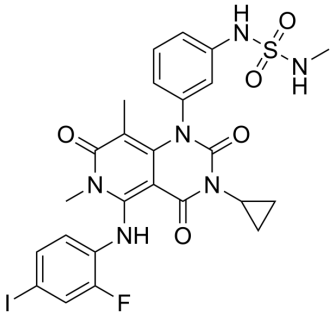
**Molecular Weight:** 666.46

**Target:** MEK

**Pathway:** MAPK/ERK Pathway

**Storage:**

| | | |
|---|---|---|
| Powder | -20°C | 3 years |
| | 4°C | 2 years |
| In solvent | -80°C | 6 months |
| | -20°C | 1 month |



## SOLVENT & SOLUBILITY

**In Vitro**

DMSO : 100 mg/mL (150.05 mM; ultrasonic and warming and heat to 60°C)

| Preparing Stock Solutions | Mass / Solvent / Concentration | 1 mg | 5 mg | 10 mg |
|---|---|---|---|---|
| | 1 mM | 1.5005 mL | 7.5023 mL | 15.0047 mL |
| | 5 mM | 0.3001 mL | 1.5005 mL | 3.0009 mL |
| | 10 mM | 0.1500 mL | 0.7502 mL | 1.5005 mL |

Please refer to the solubility information to select the appropriate solvent.

**In Vivo**

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (3.75 mM); Clear solution

## BIOLOGICAL ACTIVITY

**Description**

Trametiglue, a derivative of Trametinib (HY-10999), targets both KSR-MEK and RAF-MEK with unprecedented potency and selectivity via unique interfacial binding interactions[1].

| $IC_{50}$ & Target | MEK1 | MEK2 |
|---|---|---|

**In Vitro**

Trametiglue retains the strong binding potency and residence time of Trametinib on KSR-bound MEK[1].

Trametiglue, unlike Trametinib but similar to Avutometinib (HY-18652), enhances interactions between endogenous BRAF and MEK1[1].

Trametiglue (1 μM) demonstrates high selectivity towards MEK1 and MEK2 in direct binding assays. Trametiglue also displays high selectivity in a panel of active kinases measured for inhibition of MEK1 and MEK2 substrate phosphorylation or direct MEK1 phosphorylation by the upstream kinases[1].

Trametiglue (5 days) inhibits HCT116, A375, A549 and SK-MEL-239 cells viability with $IC_{50}$s of 0.07, 0.07, 0.12 and 0.47 nM,

respectively[1].

Trametiglue (10 nM; 10 days) inhibits colony formation in KRAS-mutant and BRAF-mutant cancer cell lines with higher potency than Trametinib[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

| | |
|---|---|
| Cell Line: | SK-MEL-239, HCT116, A549 and A375 |
| Concentration: | |
| Incubation Time: | 5 days |
| Result: | Showed $IC_{50}$s of 0.47, 0.07, 0.12 and 0.07 nM against SK-MEL-239, HCT116, A549 and A375 cells, respectively. |

Western Blot Analysis[1]

| | |
|---|---|
| Cell Line: | A549, HCT-116, A375 and SK-MEL-239 |
| Concentration: | 0.4, 0.8, 1.6, 3.1, 6.25, 12.5, 25 and 50 nM |
| Incubation Time: | 1 h |
| Result: | Inhibited the expression of pERK. And the effect was better than Trametinib. |

## REFERENCES

[1]. Khan ZM, et al. Structural basis for the action of the drug trametinib at KSR-bound MEK. Nature. 2020 Dec;588(7838):509-514.



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