# MK-8033 hydrochloride

**Cat. No.:** HY-13299A

**CAS No.:** 1283000-43-0

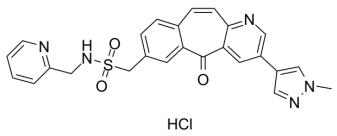
**Molecular Formula:** $C_{25}H_{22}ClN_5O_3S$

**Molecular Weight:** 507.99

**Target:** c-Met/HGFR

**Pathway:** Protein Tyrosine Kinase/RTK

**Storage:** 4°C, sealed storage, away from moisture
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)




## SOLVENT & SOLUBILITY

**In Vitro**

$H_2O$ : 7.14 mg/mL (14.06 mM; Need ultrasonic)
DMSO : 5.88 mg/mL (11.58 mM; Need ultrasonic)

**Preparing Stock Solutions**

| Solvent / Mass / Concentration | 1 mg | 5 mg | 10 mg |
|---|---|---|---|
| 1 mM | 1.9685 mL | 9.8427 mL | 19.6854 mL |
| 5 mM | 0.3937 mL | 1.9685 mL | 3.9371 mL |
| 10 mM | 0.1969 mL | 0.9843 mL | 1.9685 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: ≥ 0.59 mg/mL (1.16 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 0.59 mg/mL (1.16 mM); Clear solution

## BIOLOGICAL ACTIVITY

**Description**

MK-8033 hydrochloride is an orally active ATP competitive c-Met/Ron dual inhibitor ($IC_{50}$s: 1 nM (c-Met),7 nM (Ron)), with preferential binding to the activated kinase conformation. MK-8033 hydrochloride can be used in the research of cancers, such as breast and bladder cancers, non-small cell lung cancers (NSCLCs)[1][2].

**$IC_{50}$ & Target**

IC50: 7 nM (Ron)[1]

**In Vitro**

MK-8033 hydrochloride (Compound 11r, 10 μM) displayed 31% inhibition of CYP3A4 (cytochrome P450 3A4)[1].
MK-8033 hydrochloride (1 μM, 2 h) inhibits phosphorylation of Y1349 of c-Met ($IC_{50}$: 0.03 μM) in the c-Met dependent gastric cancer cell line GTL-16[1].
MK-8033 hydrochloride (1-10 μM, 72 h) inhibits GTL-16 cell proliferation ($IC_{50}$: 0.58 μM)[1].

MK-8033 hydrochloride binds more tightly to phosphorylated c-Met ($K_d$: 3.2 nM) than to its unphosphorylated counterpart ($K_d$: 10.4 nM), and inhibits oncogenic c-Met activation loop mutants with $IC_{50}$s ranging from 0.6 to 1 nM[1].
MK-8033 hydrochloride (0.1-10 μM, 2 h) reduces the phosphorylation of c-Met, ERK, and Akt in EBC-1 and H1993 cells[2].
MK-8033 hydrochloride (1 μM, 1 h) sensitizes EBC-1 and H1993 cells (high c-Met-expressing) to radiation[2].
MK-8033 hydrochloride (10 μM, 6 h) enhances γ-H2Ax levels in A549 cells compared to double irradiation and decreases in DNA repair[2].
MK-8033 hydrochloride (2 μM, 72 h) results in reduced cell proliferation, but modest induction of apoptosis in G-alpha protein mutant UM (uveal melanoma) cells[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[2]

| | |
|---|---|
| Cell Line: | EBC-1, H1993 cells, A549 and H460 cells |
| Concentration: | 0.1, 1, 10 μM |
| Incubation Time: | 2 h |
| Result: | Reduced the phosphorylation of c-Met, ERK, and Akt in EBC-1 and H1993 cells in a dose-dependent manner. |

**In Vivo**

MK-8033 hydrochloride (Compound 11r, oral administration, 3-100 mg/kg, twice daily for 21 days) inhibits tumor growth in GTL-16 c-Met amplified gastric tumor xenografts[1].
MK-8033 hydrochloride exhibits moderate clearance ($t_{1/2}$: 0.8 h for rats, 3.1 h for dog) and favorable bioavailability (35% for rats, 33% for dog)[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

| | |
|---|---|
| Animal Model: | Human GTL-16 c-Met amplified gastric tumor xenografts[1] |
| Dosage: | 3, 10, 30, and 100 mg/kg |
| Administration: | Oral administration, twice daily for 21 days |
| Result: | Resulted in 22, 18, 57, and 86% tumor growth inhibition at 3, 10, 30, and 100 mg/kg, respectively.<br>Inhibited c-Met (Y1349) phosphorylation. |

## CUSTOMER VALIDATION

- Nat Nanotechnol. 2021 Jul;16(7):830-839.
- Sci Rep. 2019 Dec 2;9(1):18101.

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## REFERENCES

[1]. Chandrani Chattopadhyay, et al. Simultaneous inhibition of the HGF/MET and Erk1/2 pathways affect uveal melanoma cell growth and migration. PLoS One. 2014 Feb 13;9(2):e83957.

[2]. Northrup AB, et al, Discovery of 1-[3-(1-methyl-1H-pyrazol-4-yl)-5-oxo-5H-benzo[4,5]cyclohepta[1,2-b]pyridin-7-yl]-N-(pyridin-2-ylmethyl)methanesulfonamide (MK-8033): A Specific c-Met/Ron dual kinase inhibitor with preferential affinity for the activated

[3]. Bhardwaj V, et al. C-Met inhibitor MK-8003 radiosensitizes c-Met-expressing non-small-cell lung cancer cells with radiation-induced c-Met-expression. J Thorac Oncol. 2012 Aug;7(8):1211-7.



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