# Dosimertinib-$d_5$ mesylate

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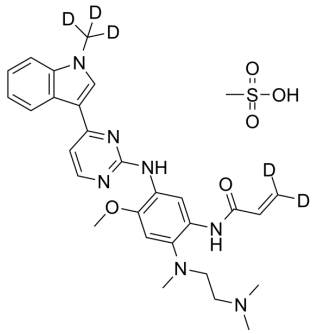
|---|---|
| **Cat. No.:** | HY-142283AS |
| **CAS No.:** | 2403760-72-3 |
| **Molecular Formula:** | $C_{29}H_{32}D_5N_7O_5S$ |
| **Molecular Weight:** | 600.74 |
| **Target:** | EGFR |
| **Pathway:** | JAK/STAT Signaling; Protein Tyrosine Kinase/RTK |
| **Storage:** | -20°C, sealed storage, away from moisture<br>* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture) |



## SOLVENT & SOLUBILITY

**In Vitro**

DMSO : 100 mg/mL (166.46 mM; ultrasonic and warming and heat to 80°C)

| Preparing Stock Solutions | Solvent / Mass / Concentration | 1 mg | 5 mg | 10 mg |
|---|---|---|---|---|
| | 1 mM | 1.6646 mL | 8.3231 mL | 16.6461 mL |
| | 5 mM | 0.3329 mL | 1.6646 mL | 3.3292 mL |
| | 10 mM | 0.1665 mL | 0.8323 mL | 1.6646 mL |

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

## BIOLOGICAL ACTIVITY

**Description**

Dosimertinib-$d_5$ (mesylate) is a potent and orally active EGFR inhibitor. Dosimertinib-$d_5$ (mesylate) decreases the expression of p-EGFR and p-ERK protein levels. Dosimertinib-$d_5$ (mesylate) shows antiproliferative and anti-tumor activity. Dosimertinib-$d_5$ (mesylate) has the potential for the research of non-small-cell lung cancer (NSCLC)[1].

**In Vitro**

Dosimertinib mesylate (compound 2h) (1, 10, 100, 100 nM; 2h) decreases the expression of p-EGFR and p-ERK protein levels in a dose-dependent manner[1].

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

Cell Proliferation Assay[1]

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| Cell Line: | A431, H1975, EGFR-L858/T790M BaF3, EGFR-del19/T790M BaF3 Cells |
| Concentration: | 0-10 μM |
| Incubation Time: | 72 h |
| Result: | Showed antiproliferative activity with $IC_{50}$s of 243.9, 28.4, 18.0, 3.5 nM for A431, H1975, EGFR-L858/T790M BaF3, EGFR-del19/T790M BaF3 cells, respectively. |

Western Blot Analysis[1]

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| Cell Line: | A431, H1975 cells |
| Concentration: | 1, 10, 100, 100 nM |
| Incubation Time: | 2 h |
| Result: | Decreased the expression of p-EGFR and p-ERK protein levels in a dose-dependent mannet when co-incubationed with 50 ng/mL EGF. |

**In Vivo**

Dosimertinib mesylate (0.75, 1.5, 3 mg/kg; oral gavage, daily for 24 days) shows anti-tumor activity in mouse[1].
Pharmacokinetic Parameters of Dosimertinib mesylate in Sprague-Dawley rats[1].

| detected compound | dosimertinib | | | |
|---|---|---|---|---|
| administration route | i.v. | i.g. | i.g. | i.g. |
| dose (mg/kg) | 2 | 2 | 6 | 12 |
| $C_0$ or $C_{max}$ (nM) | 277 ± 105 | 46.7 ± 10.7 | 113 ± 19.8 | 283 ± 137 |
| $T_{max}$ (h) | | 4.17 ± 2.56 | 4.67 ± 1.63 | 5.00 ± 1.67 |
| $t_{1/2}$ (h) | 5.40 ± 1.84 | 3.76 ± 1.08 | 3.27 ± 0.43 | 4.04 ± 1.50 |
| $AUC_{0-t}$ (nM·h) | 1070 ± 565 | 459 ± 191 | 1020 ± 313 | 2830 ± 1780 |
| CL/F (L/h/kg) | 22.3 ± 11.1 | 32.2 ± 13.6 | 19.5 ± 5.1 | 14.9 ± 6.4 |
| bioavailability (%) | | 41.2 | 29.6 | 43.0 |

Sprague-Dawley rats, 2 mg/kg iv; 2, 6, 12 mg/kg for i.g..



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| Animal Model: | 18-20 g, BALB/c nude mice (H1975 mouse xenograft model)[1] |
| Dosage: | 0.75, 1.5, 3 mg/kg |
| Administration: | Oral gavage; daily for 24 days |
| Result: | Significantly reduced tumor size with tumor growth inhibition (TGI) of 72.94% and 97.62% at 1.5, 3 mg/kg, respectively. |

## REFERENCES

[1]. Meng Y, et al. Discovery of Dosimertinib, a Highly Potent, Selective, and Orally Efficacious Deuterated EGFR Targeting Clinical Candidate for the Treatment of Non-Small-Cell Lung Cancer. J Med Chem. 2021 Jan 28;64(2):925-937.

**Caution: Product has not been fully validated for medical applications. For research use only.**

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