# Milademetan tosylate hydrate

**Cat. No.:** HY-101266B

**CAS No.:** 2095625-97-9

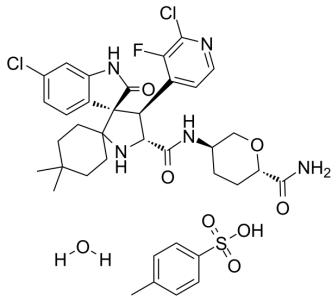
**Molecular Formula:** $C_{37}H_{44}Cl_2FN_5O_8S$

**Molecular Weight:** 808.74

**Target:** MDM-2/p53; E1/E2/E3 Enzyme; Apoptosis

**Pathway:** Apoptosis; Metabolic Enzyme/Protease

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



## SOLVENT & SOLUBILITY

**In Vitro**

DMSO : 50 mg/mL (61.82 mM; Need ultrasonic)

| Preparing Stock Solutions | Mass / Solvent / Concentration | 1 mg | 5 mg | 10 mg |
|---|---|---|---|---|
| | 1 mM | 1.2365 mL | 6.1825 mL | 12.3649 mL |
| | 5 mM | 0.2473 mL | 1.2365 mL | 2.4730 mL |
| | 10 mM | 0.1236 mL | 0.6182 mL | 1.2365 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: 5 mg/mL (6.18 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 5 mg/mL (6.18 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 5 mg/mL (6.18 mM); Clear solution

## BIOLOGICAL ACTIVITY

**Description**

Milademetan (DS-3032) tosylate hydrate is a specific and orally active MDM2 inhibitor for the research of acute myeloid leukemia (AML) or solid tumors. Milademetan (DS-3032) tosylate hydrate induces G1 cell cycle arrest, senescence and apoptosis[1][2].

**In Vitro**

Milademetan (DS-3032) can stabilize TP53 and selectively induce CDKNA1, BAX and MDM2 expression in neuroblastoma cells with wild-type TP53[3].
Milademetan (DS-3032b) treatment enhances TP53 target gene expression and induces G1 cell cycle arrest, senescence and apoptosis[3].

Mlademetan (DS-3032b, 0-2000 nM) treatment selectively inhibits viability, proliferation and migration of neuroblastoma cells with wildtype TP53 independently of MYCN status[4].

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

Cell Viability Assay[4]

| | |
|---|---|
| Cell Line: | SK-N-SH, SH-SY5Y, IMR32, IMR5 and LAN5 cell lines. |
| Concentration: | 0-2000 nM. |
| Incubation Time: | 24-72 h. |
| Result: | Reduced viability in a dose- and time-dependent manner.<br>Exhibited IC50 values of 21.9 nM, 17.7 nM, 52.63 nM, 25.7 nM and 44.1 nM in SK-N-SH, SH-SY5Y, IMR32, IMR5 and LAN5 cell lines, respectively (72 h). |

**In Vivo**

Mlademetan (DS-3032b, 50 mg/kg, oral gavage) delays tumor growth and improves survival in mice xenografted with neuroblastoma cells with functional TP53[4].

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

| | |
|---|---|
| Animal Model: | SH-SY5Y xenograft tumors in nude mice[4]. |
| Dosage: | 50 mg/kg. |
| Administration: | Oral gavage for 30 consecutive days with an alternating schedule of 4 days of daily treatment with oral gavages followed by 2 days without treatment (4+2). |
| Result: | Survival in the mouse cohort was significantly prolonged.<br>Reduced neuroblastoma xenograft tumor growth by activating TP53 signaling. |

## CUSTOMER VALIDATION

- Biomedicines. 2022, 10(3), 638.

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## REFERENCES


[1]. ARYL SULFONOHYDRAZIDES. WO 2017069289 A1.

[2]. M.M. Gounder, et al. Milademetan, an oral MDM2 inhibitor, in well-differentiated/dedifferentiated liposarcoma: results from a phase 1 study in patients with solid tumors or lymphomas. European Journal of Cancer 138S2 (2020) S1–S62.

[3]. Li, Yangbing, et al. Development of novel PROTAC Small-Molecule Degraders of MDM2 Protein and Peptidomimetic Inhibitors Targeting WDR5-MLL1 Protein-Protein Interaction.

[4]. Viktor Arnhold, et al. Reactivating TP53 signaling by the novel MDM2 inhibitor DS-3032b as a therapeutic option for high-risk neuroblastoma. ncotarget. 2018 Jan 5; 9(2): 2304–2319.

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

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