# Tirabrutinib hydrochloride

**Cat. No.:** HY-15771A

**CAS No.:** 1439901-97-9

**Molecular Formula:** $C_{25}H_{23}ClN_6O_3$

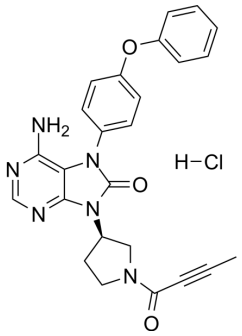
**Molecular Weight:** 490.94

**Target:** Btk; Apoptosis

**Pathway:** Protein Tyrosine Kinase/RTK; Apoptosis

**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**

DMSO : 100 mg/mL (203.69 mM; Need ultrasonic)

| Preparing Stock Solutions | Mass / Solvent / Concentration | 1 mg | 5 mg | 10 mg |
|---|---|---|---|---|
| | 1 mM | 2.0369 mL | 10.1845 mL | 20.3691 mL |
| | 5 mM | 0.4074 mL | 2.0369 mL | 4.0738 mL |
| | 10 mM | 0.2037 mL | 1.0185 mL | 2.0369 mL |

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

**In Vivo**

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (5.09 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.09 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1.79 mg/mL (3.65 mM); Clear solution

## BIOLOGICAL ACTIVITY

**Description**

Tirabrutinib (ONO-4059) hydrochloride is an orally active Bruton's Tyrosine Kinase (BTK) inhibitor (can cross the blood-brain barrier (BBB)), with an $IC_{50}$ of 6.8 nM. Tirabrutinib hydrochloride irreversibly and covalently binds to BTK and inhibits aberrant B cell receptor signaling. Tirabrutinib hydrochloride can be used in studies of autoimmune diseases and hematological malignancies[1][2][3][4].

| $IC_{50}$ & Target | | | | |
|---|---|---|---|---|
| | BMX<br>6 nM ($IC_{50}$) | BTK<br>6.8 nM ($IC_{50}$) | TEC<br>48 nM ($IC_{50}$) | TXK<br>92 nM ($IC_{50}$) |
| | BLK | ERBB4 | EGFR | JAK3 |

| | | | | |
|---|---|---|---|---|
| | 0.3 μM ($IC_{50}$) | 0.77 μM ($IC_{50}$) | 3.02 μM ($IC_{50}$) | 5.52 μM ($IC_{50}$) |
| | ERBB2<br>7.31 μM ($IC_{50}$) | | | |

**In Vitro**

Tirabrutinib hydrochloride (0.1-1000 nM or 0.001-100 nM; 72 h) inhibits the proliferation of OCI-L Y10 and SU-DHL-6 cells with $IC_{50}$s of 9.127 nM, and 17.10 nM, respectively[1].
Tirabrutinib hydrochloride (0.5, 5, 50 μM; 24, 48 h) induces SU-DHL-6 cells apoptosis needs high dosage and prolonged administration (concentration up to 50 μM and incubates for 48 h)[1].
Tirabrutinib hydrochloride (300 nM, 72 h) induces caspase-3 and PARP cleavage in TMD8 cells[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

| | |
|---|---|
| Cell Line: | SU-DHL-6 and OCI-L Y10 cells |
| Concentration: | 0.1-1000 nM; 0.001 nM-100 nM. |
| Incubation Time: | 72 h |
| Result: | Showed good anti-proliferative activity with $IC_{50}$s of 9.127 nM, and 17.10 nM for OCI-L Y10 and SU-DHL-6 cells, respectively. |

Apoptosis Analysis[1]

| | |
|---|---|
| Cell Line: | SU-DHL-6 cells |
| Concentration: | 0.5, 5, 50 μM |
| Incubation Time: | 24, 48 h |
| Result: | Induced cell apoptosis when concentration up to 50 μM and incubated for 48 h. |

Western Blot Analysis[2]

| | |
|---|---|
| Cell Line: | TMD8 cells |
| Concentration: | 300 nM |
| Incubation Time: | 72 h |
| Result: | Induced caspase-3 and PARP cleavage. |

**In Vivo**

Tirabrutinib hydrochloride (10 mg/kg; p.o.; single) is rapidly absorbed into plasma and brain, and reaches $C_{max}$ (blood $C_{max}$ =339.53 ng/mL; brain $C_{max}$ =28.9 ng/mL) 2 hours post administration[1].
Tirabrutinib hydrochloride (6, 20 mg/kg; p.o.; single daily for 3 weeks) shows inhibition of tumour growth in vivo[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

| | |
|---|---|
| Animal Model: | Male SD rats (219.0–260.5g)[1]. |
| Dosage: | 10 mg/kg |
| Administration: | Oral administration; single. |
| Result: | Pharmacokinetic Parameters of Tirabrutinib in male SD rats[1]. |

| | Plasma, $C_{max}$ (ng/mL) | Brain, $C_{max}$ (ng/mL) | Penetration rate (%, $C_{max,brain}/C_{max,plasma}$) |
|---|---|---|---|
| PO (10 mg/kg) | 339.53 | 28.9 | 8.5 |

| | |
|---|---|
| Animal Model: | Immunodeficiency (SCID) mice (mouse xenograft model)[2]. |
| Dosage: | 6, 20 mg/kg |
| Administration: | Oral administration; single daily for 3 weeks. |
| Result: | Inhibited tumour growth, and when dosage up to 20 mg/kg, a complete tumor suppression at day 14. |

## CUSTOMER VALIDATION

- Stem Cell Reports. 2019 May 14;12(5):996-1006.
- Rapid Commun Mass Spectrom. 2021 Dec 14;e9240.

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## REFERENCES

[1]. Yu H, et al. Bruton's tyrosine kinase inhibitors in primary central nervous system lymphoma-evaluation of anti-tumor efficacy and brain distribution. Transl Cancer Res. 2021 May;10(5):1975-1983.

[2]. Kozaki R, et al. Responses to the Selective Bruton's Tyrosine Kinase (BTK) Inhibitor Tirabrutinib (ONO/GS-4059) in Diffuse Large B-cell Lymphoma Cell Lines. Cancers (Basel). 2018 Apr 23;10(4):127.

[3]. Liclican A, et al. Biochemical characterization of tirabrutinib and other irreversible inhibitors of Bruton's tyrosine kinase reveals differences in on - and off - target inhibition. Biochim Biophys Acta Gen Subj. 2020 Apr;1864(4):129531.

[4]. Dhillon S. Tirabrutinib: First Approval. Drugs. 2020 Jun;80(8):835-840.

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

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