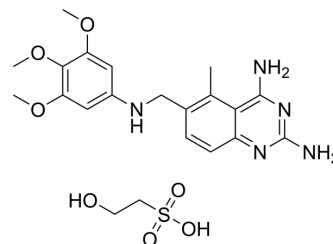


## Trimetrexate isethionate

<b>Cat. No.:</b>	HY-10373B
<b>CAS No.:</b>	82935-04-4
<b>Molecular Formula:</b>	C <sub>21</sub> H <sub>29</sub> N <sub>5</sub> O <sub>7</sub> S
<b>Molecular Weight:</b>	495.55
<b>Target:</b>	Antibiotic; Antifolate; Bacterial; Parasite; DNA/RNA Synthesis; Dihydrofolate reductase (DHFR)
<b>Pathway:</b>	Anti-infection; Cell Cycle/DNA Damage; Metabolic Enzyme/Protease
<b>Storage:</b>	Please store the product under the recommended conditions in the Certificate of Analysis.



### BIOLOGICAL ACTIVITY

<b>Description</b>	Trimetrexate (CI-898) isethionate is an antibiotic, also a potent and orally active dihydrofolate reductase (DHFR) inhibitor, reducing the production of DNA and RNA precursors and leading to cell death, with IC <sub>50</sub> values of 4.74 nM and 1.35 nM for human DHFR and <i>Toxoplasma gondii</i> DHFR. Trimetrexate isethionate can also inhibit the growth of various cancer cells. Trimetrexate isethionate can be used for researching <i>Pneumocystis carinii</i> pneumonia (PCP) and cancer <sup>[1][2][3][4][5]</sup> .																
<b>IC<sub>50</sub> &amp; Target</b>	<i>Toxoplasma</i>																
<b>In Vitro</b>	<p>Trimetrexate isethionate (0.1 μM; 18 h) completely inhibits proliferation of <i>toxoplasma</i> in murine macrophages<sup>[3]</sup>. Trimetrexate isethionate (1 μM) can cross the <i>toxoplasma</i> cell membrane and rapidly reaches high intracellular concentrations (108 pmol/10<sup>7</sup> cells within 10 min)<sup>[3]</sup>.</p> <p>Trimetrexate (0.1 mM; 24 h) inhibits cell growth by 50-60% in SNU-C4 and NCI-H630 cell lines<sup>[5]</sup>.</p> <p>Trimetrexate (1 and 10 mM; 24 h) produces lethality and inhibits DHFR in C4 cells<sup>[5]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p> <p>Cell Proliferation Assay<sup>[5]</sup></p> <table border="1"> <tr> <td>Cell Line:</td> <td>SNU-C4 and NCI-H630</td> </tr> <tr> <td>Concentration:</td> <td>0.1 mM</td> </tr> <tr> <td>Incubation Time:</td> <td>24 h</td> </tr> <tr> <td>Result:</td> <td>Inhibited cell growth by 50-60% in both cell lines.</td> </tr> </table> <p>Cell Proliferation Assay<sup>[5]</sup></p> <table border="1"> <tr> <td>Cell Line:</td> <td>C4 cells</td> </tr> <tr> <td>Concentration:</td> <td>1 and 10 mM</td> </tr> <tr> <td>Incubation Time:</td> <td>24 h</td> </tr> <tr> <td>Result:</td> <td>Produced 42% and 50% lethality at 1 and 10 mM, respectively.</td> </tr> </table>	Cell Line:	SNU-C4 and NCI-H630	Concentration:	0.1 mM	Incubation Time:	24 h	Result:	Inhibited cell growth by 50-60% in both cell lines.	Cell Line:	C4 cells	Concentration:	1 and 10 mM	Incubation Time:	24 h	Result:	Produced 42% and 50% lethality at 1 and 10 mM, respectively.
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<b>In Vivo</b>	Trimetrexate (180 mg/kg or 30 mg/kg; p.o. or i.p.; daily) isethionate extends the median survival of the <i>toxoplasma</i> infected																

mice and shows antitoxoplasma activity<sup>[3]</sup>.

Trimetrexate (0-30 mg/kg; i.v.; once daily for 5days) isethionate shows chronic toxicity in rats<sup>[4]</sup>.

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Animal Model:	Toxoplasma infected female BALB/c mice weighing about 20 g <sup>[3]</sup>
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Dosage:	180 mg/kg or 30 mg/kg
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Administration:	180 mg/kg per day orally in the drinking water or 30 mg/kg per day i.p.
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Result:	Extended the median survival of the infected mice to 10 d (p.o.) or 19 d (i.p.).
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Animal Model:	Charles River Wistar CrI(WI)BR rats weighing approximately 150 to 200 g <sup>[4]</sup>
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Dosage:	0, 1, 10, or 30 mg/kg
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Administration:	Intravenous injection, once daily for 5 consecutive days followed by a 23-day recovery period
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Result:	Showed chronic toxicity, the testicular changes persisting during the course of multiple cycles of dosing were not reversible within 21 days, but required an additional 56 days for essentially complete recovery.
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## REFERENCES

[1]. Hopper AT, et al. Discovery of Selective Toxoplasma gondii Dihydrofolate Reductase Inhibitors for the Treatment of Toxoplasmosis. J Med Chem. 2019 Feb 14;62(3):1562-1576.

[2]. Fulton, B., et al. Trimetrexate. Drugs 49, 563–576 (1995).

[3]. Allegra CJ, et al. Potent in vitro and in vivo antitoxoplasma activity of the lipid-soluble antifolate trimetrexate. J Clin Invest. 1987 Feb;79(2):478-82.

[4]. Dethloff LA, et al. Chronic toxicity of the anticancer agent trimetrexate in rats. Fundam Appl Toxicol. 1992 Jul;19(1):6-14.

[5]. Grem JL, Voeller DM, Geoffroy F, Horak E, Johnston PG, Allegra CJ. Determinants of trimetrexate lethality in human colon cancer cells. Br J Cancer. 1994 Dec;70(6):1075-84.

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

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