

## Product Data Sheet

Product Name: Teriflunomide (A 77-1726)

Cat. No.: GC17919

### Chemical Properties

Cas. No. 108605-62-5, 163451-81-8

Chemical Name (Z)-2-cyano-3-hydroxy-N-[4-(trifluoromethyl)phenyl]but-2-enamide

SMILES CC(=C(C#N)C(=O)NC1=CC=C(C=C1)C(F)(F)F)O

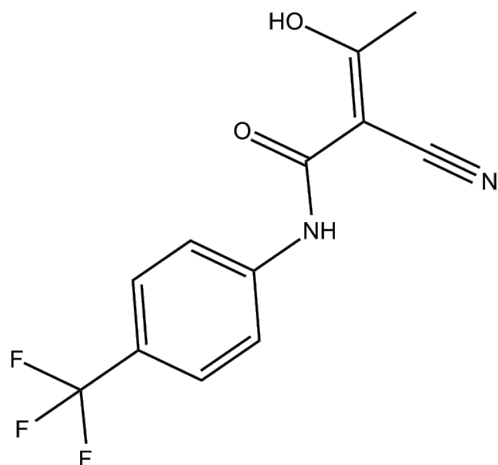
Formula  $C_{12}H_9F_3N_2O_2$  M.Wt 270.21

Solubility  $\geq 13.5\text{mg/mL}$  in DMSO Storage Store at  $-20^\circ\text{C}$

General tips For obtaining a higher solubility, please warm the tube at  $37^\circ\text{C}$  and shake it in the ultrasonic bath for a while. Stock solution can be stored below  $-20^\circ\text{C}$  for several months.

Shipping Condition Evaluation sample solution: ship with blue ice. All other available size: ship with RT, or blue ice upon request.

Structure



### Protocol

#### Cell experiment [1]:

Cell lines Vero cells (CCL-81), immortalized human hepatocyte cells (imHC), and human epithelial type 2 cells (HEp-2; CCL-23)

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|-------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Preparation Method            | Vero, imHC and HEp-2 cells were cultivated in Minimum Essential Medium (Vero, HEp-2) or DMEM/F12 (imHC) supplemented with 10% heat-inactivated FBS at 37°C, 5% CO <sub>2</sub> . For antiviral assay, cells were inoculated with DENV-2, ZIKV, CHIKV, IAV H1N1 or RSV-A for 2h, then replaced with 2% FBS media containing two-fold serial dilutions of Teriflunomide; CHIKV-infected cells were incubated for 1 day and other infected cells for 2 days before viral supernatant collection. Cytotoxicity was assessed by incubating uninfected cells with Teriflunomide in 2% FBS media for 48h.                                                                                                                                                                    |
| Reaction Conditions           | 5.5–25.2μM; 1–2 days                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| Applications                  | Teriflunomide dose-dependently reduced viral titers across all tested RNA viruses, with IC <sub>50</sub> values of 5.5μM (DENV-2, imHC), 11.1μM (ZIKV, imHC), 19.3μM (CHIKV, Vero), 25.2μM (IAV H1N1, Vero) and 11.2μM (RSV-A, HEp-2). CC <sub>50</sub> values were 67.43μM (imHC), 378.3μM (Vero) and >200μM (HEp-2), giving selective indices of 12.24, 6.10, 19.60, 15.00 and >17.94.                                                                                                                                                                                                                                                                                                                                                                              |
| <b>Animal experiment [2]:</b> |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| Animal models                 | Swiss albino mice (25–30g).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| Preparation Method            | Mice were divided into 7 groups: vehicle control, scopolamine (2mg/kg; i.p.)+0.1% CMC (p.o.), donepezil (3mg/kg; i.p.)+scopolamine, Teriflunomide (10–20mg/kg; p.o.)+scopolamine, LY294002 (25μg/kg; i.p.)+0.1% CMC (p.o.), and LY294002+Teriflunomide (20mg/kg; p.o.). All treatments were given continuously for 9 days, with scopolamine injected on days 7–9 (i.p.; 30min after donepezil/Teriflunomide), and LY294002 administered on days 7–9 (Teriflunomide given 30min before LY294002 on day 9). Behavioral tests (Morris water maze, Y-maze, open field test, rotarod) were performed on days 7 and 9. On day 9 post-behavior, mice were anesthetized, blood collected for serum TNF-α ELISA, then sacrificed for brain harvesting to assess GSH and TBARS. |

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Dosage form 10, 20mg/kg; p.o.; 9 days

Applications Teriflunomide (20mg/kg) significantly reduced escape latency in the MWM, increased spontaneous alternation percentage in the Y-maze, elevated square crossings in the OFT and prolonged retention time on the rotarod in scopolamine-treated mice, with 10mg/kg showing effects in OFT and rotarod but weaker in MWM and Y-maze. Teriflunomide (20mg/kg) upregulated brain GSH, downregulated brain TBARS and serum TNF- $\alpha$  in the scopolamine model. In LY294002-treated mice, Teriflunomide (20mg/kg) abrogated LY294002-induced increases in MWM escape latency and serum TNF- $\alpha$ , and LY294002-induced reductions in Y-maze spontaneous alternation and brain GSH, with no significant effect on TBARS.

### References:

- [1] Sirihongthong T, Jitobaom K, Boonarkart C, et al. In Vitro Synergistic Antiviral Effects of  $\beta$ -D-N4-hydroxycytidine and Teriflunomide in Combination against a Broad Range of RNA Viruses. J Med Virol. 2025 Jul;97(7):e70488.
- [2] Kanika, Singh L. Mitigating cognitive deficits with teriflunomide: unraveling PI3K-modulated behavioral outcomes in mice. Mol Biol Rep. 2024 May 9;51(1):572.

### Background

Teriflunomide (A 77-1726) is a novel, orally active dihydroorotate dehydrogenase (DHODH) inhibitor that blocks de novo pyrimidine synthesis. Teriflunomide inhibits DHODH to block de novo pyrimidine synthesis, thereby suppressing the activation of proliferating T cells and B cells, and reduces inflammation through immunomodulation. Teriflunomide can be used in research related to multiple sclerosis and rheumatoid arthritis<sup>[1-4]</sup>.

In vitro, Teriflunomide (5.5–25.2 $\mu$ M) acts on imHC cells infected with Dengue virus (DENV-2) or Zika virus (ZIKV), Vero cells infected with Chikungunya virus (CHIKV) or Influenza virus (IAV H1N1), and HEp-2 cells infected with respiratory syncytial virus (RSV-A) (virus infection for 2h followed by

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replacement with drug-containing medium; CHIKV-infected cultures were incubated for 1 day, while the others were incubated for 2 days). Teriflunomide significantly reduced the titers of all tested viruses<sup>[5]</sup>. Teriflunomide (100–500 $\mu$ M) was applied to human multiple myeloma RPMI 8226 cells and human skin fibroblast BJ cells for 24h, with some conditions combined with uridine (50, 500 $\mu$ M). Teriflunomide concentration-dependently decreased cell viability, arrested the cell cycle at the G2/M phase, increased the proportion of subG1 phase cells, and induced early and late apoptosis<sup>[6]</sup>.

In vivo, Teriflunomide (10, 20mg/kg; p.o.) was co-administered with scopolamine (2mg/kg; i.p.) to cognitively impaired Swiss mice and to LY294002 (25 $\mu$ g/kg)-treated PI3K inhibition model mice for 9 consecutive days. Teriflunomide significantly improved behavioral parameters including Morris water maze escape latency, Y-maze spontaneous alternation rate, open-field crossing number, and rotarod retention time; it upregulated brain GSH levels, downregulated brain TBARS and serum TNF- $\alpha$  levels, and reversed LY294002-induced memory impairment, GSH reduction, and TNF- $\alpha$  elevation<sup>[7]</sup>. Teriflunomide (10mg/kg/day) was administered via drinking water to C57BL/6N mice carrying a human PLP1 mutation, with three treatment regimens: preventive (starting at 4 months of age for 150 or 330 days), therapeutic (starting at 10 months of age for 150 days), and treatment cessation (drug withdrawal after 75 days followed by observation for 75 days). Teriflunomide significantly reduced the number of CD8<sup>+</sup> cytotoxic effector T cells in the central nervous system and promoted the proliferation of CD8<sup>+</sup>CD122<sup>+</sup>PD-1<sup>+</sup> regulatory T cells. Preventive administration alleviated axonal pathology in the optic tectum system and retinal ganglion cell loss, and slowed thinning of the innermost retinal complex layer. No neuroinflammatory rebound occurred after treatment cessation, and histological improvements were maintained for at least 75 days. When administered after disease onset, Teriflunomide halted progressive axonal perturbation and promoted recovery of dendritic arborization in surviving retinal ganglion cells<sup>[8]</sup>.

### References:

- [1] Paik J. Teriflunomide: Pediatric First Approval. *Paediatr Drugs*. 2021 Nov;23(6):609-613.
- [2] Scott LJ. Teriflunomide: A Review in Relapsing-Remitting Multiple Sclerosis. *Drugs*. 2019 Jun;79(8):875-886.
- [3] Costa GD, Comi G. Teriflunomide: an oral therapy for first-line treatment of children and adolescents living with relapsing-remitting multiple sclerosis. *Expert Rev Neurother*. 2023 Jul-Dec;23(8):681-687.
- [4] Lang P, Geertsens SS, Lublin AL, et al. *In vitro* evaluation of the activity of teriflunomide against

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SARS-CoV-2 and the human coronaviruses 229E and OC43. Biochem Biophys Rep. 2023 Mar;33:101395.

[5] Sirihongthong T, Jitobaom K, Boonarkart C, et al. In Vitro Synergistic Antiviral Effects of  $\beta$ -D-N4-hydroxycytidine and Teriflunomide in Combination against a Broad Range of RNA Viruses. J Med Virol. 2025 Jul;97(7):e70488.

[6] Adamczuk G, Humeniuk E, Iwan M, et al. The Mitochondria-Independent Cytotoxic Effect of Leflunomide on RPMI-8226 Multiple Myeloma Cell Line. Molecules. 2021 Sep 17;26(18):5653.

[7] Kanika, Singh L. Mitigating cognitive deficits with teriflunomide: unraveling PI3K-modulated behavioral outcomes in mice. Mol Biol Rep. 2024 May 9;51(1):572.

[8] Groh J, Hörner M, Martini R. Teriflunomide attenuates neuroinflammation-related neural damage in mice carrying human PLP1 mutations. J Neuroinflammation. 2018 Jul 3;15(1):194.

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