Tofacitinib Prodrug-1

Cat. No.: HY-145829

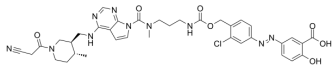
Molecular Formula: $C_{36}H_{39}ClN_{10}O_7$

Molecular Weight: 759.21

Target: JAK; Apoptosis

Pathway: Epigenetics; JAK/STAT Signaling; Stem Cell/Wnt; Apoptosis

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

Tofacitinib Prodrug-1 is an effective and oral active prodrug to mitigate the systemic adverse effects of Tofacitinib. Tofacitinib Prodrug-1 can effectively attenuate the oxazolone-induced colitis in mice model with low toxicity. Tofacitinib Prodrug-1 is a potential drug candidate for the treatment of ulcerative colitis[1].

In Vitro

Tofacitinib Prodrug-1 (compound 20g) (1 mM; 12 hours at 37 °C) is not obviously degraded from 0 to 12 hours in simulated gastric and intestinal fluid[1].

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

In Vivo

Tofacitinib Prodrug-1 (22.5 mg/kg; p.o.) can decrease the systemic exposure of tofacitinib by releasing the parent drug Tofacitinib into the circulation slowly[1].

Tofacitinib Prodrug-1 (22.5 mg/kg; p.o.) can increase intestinal exposure to improve the therapeutic effect of Tofacitinib[1].

Tofacitinib Prodrug-1 (1.5 mg/kg; p.o.; twice daily, for 4 days) can effectively attenuate the oxazolone-induced colitis in mice [1].

Tofacitinib Prodrug-1 (1.5 mg/kg; i.g.; twice daily, for 4 days) has no apparent influence on systemic immunosuppression in normal mice, which could decrease the risk of infection associated with Tofacitinib[1].

Tofacitinib Prodrug-1 (2000 mg/kg; i.g.; single) has low toxicity and was tolerated at an oral dose of 2000 mg/kg, and no significant change was observed in biochemical parameters and organ indexes[1].

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

Animal Model:	Male SD rats (5-6 weeks, 220-250 g, n=6) (pharmacokinetic)[1]
Dosage:	22.5 mg/kg
Administration:	p.o.; blood were taken at 1, 2, 4, 6, 8, 12, 14, and 20 hours
Result:	Decreased the systemic exposure of tofacitinib by releasing the parent drug tofacitinib into the circulation slowly.

Animal Model:	Male BALB/c mice (5-6 weeks, 25-30 g, n = 6)[1]
Dosage:	22.5 mg/kg

Administration:	p.o.; blood and intestinal tissues were taken at 0.5, 1, 2, 3, 4, 6, 9, and 12 hours
Result:	Increased intestinal exposure to improve the therapeutic effect of tofacitinib.

Animal Model:	Male BALB/c mice (5-6 weeks, 25-28 g, n=7-9)[1]
Dosage:	1.5 mg/kg
Administration:	p.o.; twice daily, for 4 days
Result:	Tofacitinib Prodrug-1 could effectively attenuate the oxazolone-induced colitis in mice.

Animal Model:	Male BALB/c mice (5-6 weeks, 25-28 g, n = 10)[1]
Dosage:	1.5 mg/kg
Administration:	i.g.; twice daily, for 4 days
Result:	Had no apparent influence on systemic immunosuppression in normal mice, which could decrease the risk of infection associated with tofacitinib.

Animal Model:	Kunming mice (18-22 g; n = 10)[1]
Dosage:	2000 mg/kg
Administration:	i.g.; single
Result:	Had low toxicity and was tolerated at an oral dose of 2000 mg/kg, and no significant change was observed in biochemical parameters and organ indexes.

REFERENCES

[1]. Zhao J, et al. Discovery of a Colon-Targeted Azo Prodrug of Tofacitinib through the Establishment of Colon-Specific Delivery Systems Constructed by 5-ASA-PABA-MAC and 5-ASA-PABA-Diamine for the Treatment of Ulcerative Colitis. J Med Chem. 2022;65(6):4926-4948.

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