# BMS-986339

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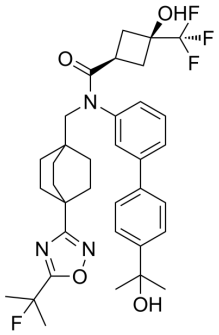
| **Cat. No.:** | HY-150787 |
| **CAS No.:** | 2477873-64-4 |
| **Molecular Formula:** | $C_{35}H_{41}F_4N_3O_4$ |
| **Molecular Weight:** | 643.71 |
| **Target:** | FXR; Cytochrome P450 |
| **Pathway:** | Metabolic Enzyme/Protease |
| **Storage:** | Please store the product under the recommended conditions in the Certificate of Analysis. |




## BIOLOGICAL ACTIVITY

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| **Description** | BMS-986339 is an orally active, potent FXR agonist. BMS-986339 forms H-bond with His298 and ASN287 residues. BMS-986339 can be used in the research of primary biliary cirrhosis (PBC), primary sclerosing cholangitis (PSC), and nonalcoholic steatohepatitis (NASH), anti-fibrosis[1]. |

| **$IC_{50}$ & Target** | CYP2C8 | CYP2C9 |
|---|---|---|
| | 8 μM ($IC_{50}$) | 13.5 μM ($IC_{50}$) |

**In Vitro**

BMS-986339 (compound 32, 0.1 nM-10 μM, 24 h) reduces activation of genes expressing BSEP (bile salt export pump) in Huh-7 cells, and FGF19 in hepatocytes[1].

BMS-986339 inhibits cytochrome P450 activity ($IC_{50}$: 8 μM ($CYP_{2C8}$), 13.5 μM ($CYP_{2C9}$)), and inhibits hERG channel in a patch clamp assay ($IC_{50}$: 4.5 μM)[1].

BMS-986339 inhibits transporters OATP1B3 and BSEP with $IC_{50}$ values of 1.44 and 1.5 μM, and hUGT1A1 ($IC_{50}$: 4.85 μM)[1].

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

**In Vivo**

BMS-986339 (compound 32, p.o., 10 mg/kg, once daily for 9 days) induces Fgf15 production, and shows antifibrotic efficacy in mouse bile duct ligation (BDL) model[1].

BMS-986339 (p.o. or i.v., 5 mg/kg or 1 mg/kg) exhibits low clearance and a long elimination half-life in mice and rats[1].

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

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| Animal Model: | Mouse bile duct ligation (BDL) model[1] |
| Dosage: | 0.3, 1, 3, and 10 mg/kg, once daily for 9 days. |
| Administration: | Oral administration |
| Result: | Induced Fgf15 and SHP (small heterodimer partner) gene expression to a similar extent in the ileum.<br>Decreased the ratio of hydroxyproline to the total protein content, and decreased the collagen levels. |

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| Animal Model: | Male C57BL6 mice, male Sprague-Dawley rat (pharmacokinetic assay)[1] |

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| Dosage: | 5 mg/kg or 1 mg/kg |
| Administration: | Oral administration, intravenous injection |
| Result: | Pharmacokinetic profile of BMS-986339 (compound 32). |

| parameter | male C57BL6 mice | male Sprague-Dawley rat |
|---|---|---|
| dose (mg/kg) i.v. | 1 | 1 |
| dose (mg/kg) p.o. | 5 | 2 |
| Vss (L/kg) i.v. | 2.2 | 5.2 |
| AUCtotal (μM•h) i.v. | 16.4 | 6.6 |
| AUCtotal (μM•h) p.o. | 56.6 | 5.8 |
| $t_{1/2}$ h (i.v.) | 16 | 18 |
| $F_{p.o.}$ | 69 | 40 |

## REFERENCES

[1]. Susheel J Nara, et al. Discovery of BMS-986339, a Pharmacologically Differentiated Farnesoid X Receptor Agonist for the Treatment of Nonalcoholic Steatohepatitis. J Med Chem. 2022 Jul 14;65(13):8948-8960.



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