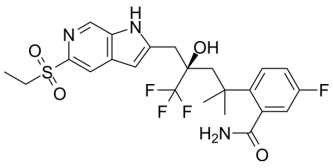
BI 653048

Cat. No.:	HY-12946
CAS No.:	1198784-72-3
Molecular Formula:	$C_{23}H_{25}F_4N_3O_4S$
Molecular Weight:	515.52
Target:	Glucocorticoid Receptor; HCV Protease; Cytochrome P450
Pathway:	Immunology/Inflammation; Vitamin D Related/Nuclear Receptor; Anti-infection; Metabolic Enzyme/Protease
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

BI 653048 is a selective and orally active nonsteroidal glucocorticoid (GC) agonist with an IC_{50} value of 55 nM[1]. BI 653048 inhibits CP1A2, CYP2D6, CYP2C9, CYP2C19 and CYP3A4 isoforms' activity and reduces affinity for the hERG ion channel (IC_{50} >30 μM)[2]. BI 653048 is extracted from patent WO2005028501A1 (Compound 103), is also a HCV NS3 protease inhibitor that can reduce viral loads infected with the hepatitis C virus[3].

IC_{50} & Target

CYP1A2 50 μM (IC_{50})	CYP2D6 41 μM (IC_{50})	CYP2C9 12 μM (IC_{50})	CYP2C19 9 μM (IC_{50})
CYP3A4 8 μM (IC_{50})			

In Vitro

BI 653048 exhibits an improved drug-like properties, inhibits CP1A2 ,CYP2D6 ,CYP2C9, CYP2C19 and CYP3A4 with IC_{50} values of 50 μM, 41 μM, 12 μM, 9 μM,and 8 μM, respectively[2].

BI 653048 reduces affinity for the hERG ion channel with an IC_{50}>30 μM in recombinant HEK293 cells expressing the human ERG potassium channel[2].

BI 653048 inhibits TNF-stimulated IL-6 production in mouse RAW cells with an IC_{50} value of 100 nM[2].

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

In Vivo

BI 653048 (oral administration; 3, 10, and 30 mg/kg) at 3 mg/kg has nonsignificant decreases for all measured histology parameters (ankle inflammation, pannus formation, cartilage damage, and bone resorption), Mid-dose (10 mg/kg) treatment significantly decreases pannus and bone resorption (33%) as well as summed scores (27%), while at high dose (30 mg/kg), all parameters are significantly decreased (87–96%). The ED_{50} value for the summed scores is 14 mg/kg[2].

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

Animal Model:	Mice[2]
Dosage:	3, 10, and 30 mg/kg
Administration:	Oral administration
Result:	Exhibits significant decreases for all measured histology parameters at high doses.

REFERENCES

[1]. Reeves JT, et al. Development of a large scale asymmetric synthesis of the glucocorticoid agonist BI 653048 BS H3PO4.J Org Chem. 2013 Apr 19;78(8):3616-35.

[2]. Montse Llinas-Brunet, et al. Latest bibliographic data on file with the International Bureau

[3]. Harcken C, et al. Optimization of drug-like properties of nonsteroidal glucocorticoid mimetics and identification of a clinical candidate.ACS Med Chem Lett. 2014 Nov 20;5(12):1318-23.

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