Product Name: JNJ 303

Revision Date: 6/30/2018

Product Data Sheet

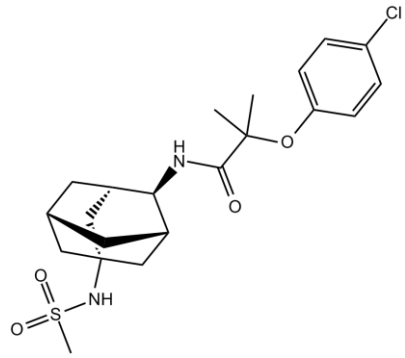
Chemical Properties

Product Name: JNJ 303

Cas No.: 878489-28-2

M.Wt: 440.98

Formula: C21H29ClN2O4S



Chemical Name: 2-(4-chlorophenoxy)-2-methyl-N-((1R,2s,3S,5s,7s)-5-(methylsulfonamido)adamantan-2-yl)propanamide

Canonical SMILES: ClC1=CC=C(C=C1)OC(C)(C)C(N[C@@H]([C@@H]2C3)[C@H](C4)C[C@@]3(C[C@H]4C2)NS(=O)(C)=O)=O

Solubility: <11.02mg/ml in DMSO

Storage: Store at -20°C

General tips: For obtaining a higher solubility , please warm the tube at 37° C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20° C for several months.

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

Biological Activity

Targets : Membrane Transporter/Ion Channel

Pathways: Potassium Channel

Description:

JNJ 303 is a potent blocker of the slow component of delayed rectifier potassium current (IKs) [1] with an IC50 value of 0.064 μM [2].
Accompanied by the transient outward current (Ito), IKs channel is a main potassium channel that affects cardiac repolarisation and thus the length of the QT interval [2].
Dofetilide accompanied by JNJ 303 resulted in an additional 80% field potential prolongation.

Sotalol administration with JNJ 303 in hPSC-CM resulted in an additional maximum prolongation of field potential (FP) duration of ~25% of cells. JNJ 303 treatment in a patient-derived hiPSC line led to a maximum 30% prolongation, this prolongation is significantly more than that in the control hPSC-CM. JNJ 303 had minor effect on the repolarization of spontaneously beating human pluripotent stem cells (hPSC-CM) [1].
The addition of IKs blockade to IKr blockade gave at least additive QT prolongation and even torsades de pointes (TdP). Treatment with JNJ 303 resulted in spontaneous events of a "pause-dependent" TdP nature in an anaesthetised dog model. Treatment with JNJ 303 made at least two animals die unexpectedly in early pharmacokinetic or pharmacological studies. Compared with other tested sulphonamide analogue in an adrenergic-dependent TdP dog model, JNJ 303 bore a much reduced IKr (hERG, rapidly activating delayed inward rectifier potassium channel) blocking activity with an IC50 value of 12,640 nM and a higher potency on the 11β-hydroxysteroid dehydrogenase-1 (HSD1) [2].

***Reference**:*

[1]. S. R. Braam, L. Tertoolen, S. Casini, et al. Repolarization reserve determines drug responses in human pluripotent stem cell derived cardiomyocytes. Stem Cell Research, 2013, 10:48-56.
[2]. Rob Towart, Joannes T.M. Linders, An N. Hermans, et al. Blockade of the IKs potassium channel: An overlooked cardiovascular liability in drug safety screening Journal of Pharmacological and Toxicological Methods, 2009, 60: 1-10.

Caution

FOR RESEARCH PURPOSES ONLY.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

Specific storage and handling information for each product is indicated on the product datasheet. Most ApexBio products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Shortterm storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.

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