

Product Data Sheet

Product Name: E-4031
Cat. No.: GC13490

Chemical Properties

Cas. No. 113558-89-7

Chemical Name N-(4-(1-(2-(6-methylpyridin-2-yl)ethyl)piperidine-4-carbonyl)phenyl)methanesulfonamide

SMILES CC1=NC(CCN2CCC(C(C3=CC=C(NS(C)(=O)=O)C=C3)=O)CC2)=CC=C1

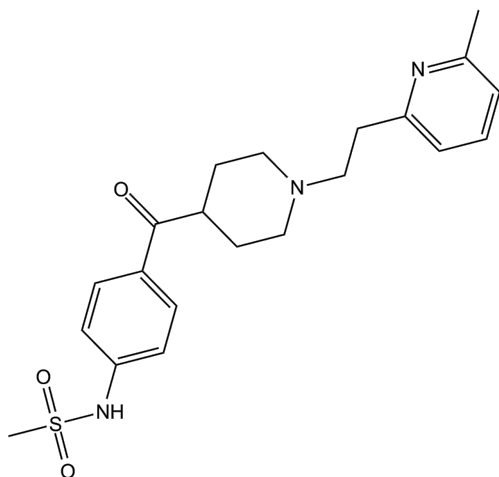
Formula $C_{21}H_{27}N_3O_3S$ M.Wt 401.52

Solubility 25mg/mL in DMSO, 0.3mg/mL in DMF Storage 4°C, sealed storage, away from moisture

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.

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

Structure



Caution: Product has not been fully validated for medical applications. For research use only.

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Background

IC50: 7.7 nM for hERG

E-4031 is an antiarrhythmic agent blocking the ATP-sensitive potassium channel.

ATP-sensitive potassium channels are distributed in tissues widely including muscle, pancreatic beta cells and brain. Their activity is regulated by adenine nucleotides, being activated by falling ATP and rising ADP levels. Thus, ATP-sensitive potassium channels link cellular metabolism with membrane excitability.

In vitro: It has been reported that E-4031 could induce EADs or TdP, and such induction correlated with a significant increase in variability of repolarization. In addition, E-4031 at 0.1 μ M was able to significantly prolong cycle length, action potential duration, and depolarized maximum diastolic potential. E-4031 could also reduce the upstroke velocity of the action potential as well as the diastolic depolarization rate [1].

In vivo: Animal study showed that E-4031 at 0.01 and 0.1 mg/kg could provide effective in-vitro plasma concentrations to significantly inhibit I_{Kr} and thus delayed the repolarization beyond the initiation of diastole, leading to the inversion of electro-mechanical coupling, which provides an ideal proarrhythmic substrate [2]. Another study found that E-4031 could prolong QT interval and ARI in all LV layers, though the magnitude of prolongation was greatest in Mid, particularly during bradycardia [3].

Clinical trial: Up to now, E-4031 is still in the preclinical development stage.

References:

- [1]. Verheijck EE, et al. Effects of delayed rectifier current blockade by E-4031 on impulse generation in single sinoatrial nodal myocytes of the rabbit. *Circ Res.* 1995 Apr;76(4):607-15.
- [2]. Izumi-Nakaseko H, et al. Effects of selective I_{Kr} channel blockade by E-4031 on ventricular electro-mechanical relationship in the halothane-anesthetized dogs. *Eur J Pharmacol.* 2014 Oct 5;740:263-70.
- [3]. Izumi D, et al. Effects of bepridil versus E-4031 on transmural ventricular repolarization and inducibility of ventricular tachyarrhythmias in the dog. *Pacing Clin Electrophysiol.* 2010 Aug;33(8):950-9.

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