

Product Data Sheet

Product Name: Darifenacin HBr

Cat. No.: GC15772

Chemical Properties

Cas. No. 133099-07-7

Chemical Name 2-[(3S)-1-[2-(2,3-dihydro-1-benzofuran-5-yl)ethyl]pyrrolidin-3-yl]-2,2-diphenylacetamide; hydrobromide

SMILES C1CN(CC1C(C2=CC=CC=C2)(C3=CC=CC=C3)C(=O)N)CCC4=CC5=C(C=C4)OCC5.Br

Formula C₂₈H₃₁BrN₂O₂

M.Wt 507.48

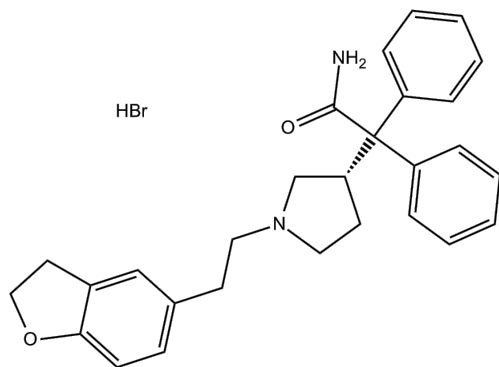
Solubility ≥ 20.2mg/mL in DMSO

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.

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

Structure



Background

DarifenacinHBr(UK88525) is a selective M3 muscarinic receptor antagonist with pKi of 8.9 [1].

The muscarinic acetylcholine receptor, also known as cholinergic/acetylcholine receptor M3, or the muscarinic 3, is a muscarinic acetylcholine receptor encoded by the human gene CHRM3. The M3 muscarinic receptors are widely expressed in tissues such as smooth muscles, the endocrine glands, the exocrine glands, lungs and pancreas. M3 muscarinic receptor is involved in

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smooth muscle contraction and increases glandular secretions [2].

In vitro: In a model of the blood-brain barrier (BBB) and blood-ocular barrier (BOB), Darifenacin was a substrate for the P-gp drug efflux transporter. Darifenacin increased ATPase activity in a concentration-dependent manner in P-gp membranes with an ED50 value of 1.6 μ M. Darifenacin treatment (100 nM) showed a significantly greater permeability for darifenacin in the basolateral to apical direction resulting in an efflux ratio in BBMEC monolayers of approximately 2.6 [3].

In vivo: Darifenacin dose-dependently inhibited the amplitude of volume-induced bladder contractions (VIB CAMP), producing 35% inhibition at dose of 283.3 nmol/kg and maximal inhibition of approximately 50–55% [1]. In female Sprague-Dawley rats, administration of darifenacin (0.1 mg/kg i.v.) reduced bladder afferent activity in A δ and C fibers. The decrease of afferent spikes in C fibers was more pronounced than that in A δ fibers [3]. In patients with overactive bladder (OAB), darifenacin at a dose of 7.5 mg and 15 mg exhibited a rapid onset of effect, with significant improvement compared with placebo being seen for most parameters at the first clinic visit (week 2). Darifenacin administration (7.5 mg and 15 mg, daily) reduced the number of incontinence episodes per week from baseline by 67.7% and 72.8% respectively compared with 55.9% with placebo in patients with overactive bladder (OAB). Darifenacin (7.5 mg and 15 mg, daily) also showed significantly superior to placebo for improvements in micturition frequency, bladder capacity, frequency of urgency, number of incontinence episodes and severity of urgency leading to a change in clothing or pads in patients with overactive bladder (OAB) [4].

References:

- [1]. Hegde SS1, Choppin A, Bonhaus D, Briaud S, Loeb M, Moy TM, Loury D, Eglen RM. Functional role of M2 and M3 muscarinic receptors in the urinary bladder of rats in vitro and in vivo. *Br J Pharmacol.* 1997 Apr;120(8):1409-18.
- [2]. Brann MR1, Ellis J, Jrgensen H, Hill-Eubanks D, Jones SV. Muscarinic acetylcholine receptor subtypes: localization and structure/function. *Prog Brain Res.* 1993;98:121-7.
- [3]. Miller DW1, Hinton M, Chen F. Evaluation of drug efflux transporter liabilities of darifenacin in cell culture models of the blood-brain and blood-ocular barriers. *Neurourol Urodyn.* 2011 Nov;30(8):1633-8. doi: 10.1002/nau.21110. Epub 2011 Aug 8.
- [4]. Haab F1, Stewart L, Dwyer P. Darifenacin, an M3 selective receptor antagonist, is an effective and well-tolerated once-daily treatment for overactive bladder. *Eur Urol.* 2004 Apr;45(4):420-9; discussion 429.

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