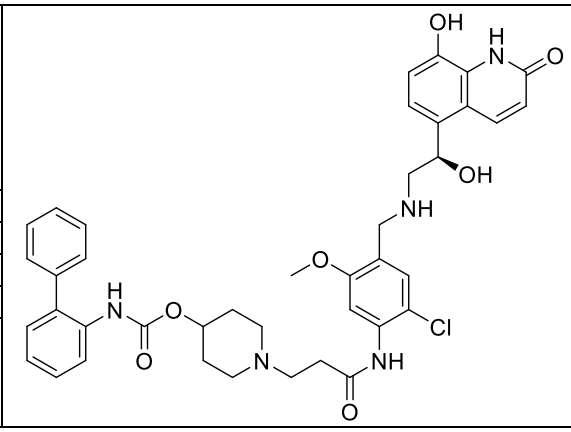
Product data sheet

MedKoo Cat#: 319652 Name: Batefenterol CAS#: 743461-65-6 (free base) Chemical Formula: $C_{40}H_{42}ClN_5O_7$ Exact Mass: 739.2773 Molecular Weight: 740.254	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
Batefenterol, also known as GSK961081 and TD-5959, is a Muscarinic Antagonist and β2-Agonist possessing both muscarinic antagonist (MA) and β2-adrenoceptor agonist (BA) properties (MABA). GSK-961081 displayed high affinity for hM2 (Ki = 1.4 nM), hM3 muscarinic receptors (Ki = 1.3 nM) and hβ2-adrenoceptors (Ki = 3.7 nM). GSK-961081 behaved as a potent hβ2-adrenoceptor agonist (EC50 = 0.29 nM for stimulation of cAMP levels) with 440- and 320-fold functional selectivity over hβ1- and hβ3-adrenoceptors, respectively.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	67.0	90.51

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.35 mL	6.75 mL	13.51 mL
5 mM	0.27 mL	1.35 mL	2.70 mL
10 mM	0.14 mL	0.68 mL	1.35 mL
50 mM	0.03 mL	0.14 mL	0.27 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Hegde SS, Hughes AD, Chen Y, Steinfeld T, Jasper JR, Lee TW, McNamara A, Martin WJ, Pulido-Rios MT, Mammen M. Pharmacologic characterization of GSK-961081 (TD-5959), a first-in-class inhaled bifunctional bronchodilator possessing muscarinic receptor antagonist and β2-adrenoceptor agonist properties. J Pharmacol Exp Ther. 2014 Oct;351(1):190-9. doi: 10.1124/jpet.114.216861. Epub 2014 Aug 6. PMID: 25100753.

In vivo study

1. Hegde SS, Hughes AD, Chen Y, Steinfeld T, Jasper JR, Lee TW, McNamara A, Martin WJ, Pulido-Rios MT, Mammen M. Pharmacologic characterization of GSK-961081 (TD-5959), a first-in-class inhaled bifunctional bronchodilator possessing muscarinic receptor antagonist and β2-adrenoceptor agonist properties. J Pharmacol Exp Ther. 2014 Oct;351(1):190-9. doi: 10.1124/jpet.114.216861. Epub 2014 Aug 6. PMID: 25100753.

Product data sheet

7. Bioactivity

Biological target:

Batefenterol (GSK961081;TD-5959) is a novel muscarinic receptor antagonist and β2-adrenoceptor agonist; displays high affinity for hM2, hM3 muscarinic and hβ2-adrenoceptor with Ki values of 1.4, 1.3 and 3.7 nM, respectively.

In vitro activity

The objective of the present studies was to characterize the pharmacologic properties of GSK-961081 [TD-5959; (R)-1-(3-((2-chloro-4-(((2-hydroxy-2-(8-hydroxy-2-oxo-1,2-dihydroquinolin-5-yl)ethyl)amino)methyl)-5-methoxyphenyl)amino)-3-oxopropyl) piperidin-4-yl [1,1'-biphenyl]-2-ylcarbamate], a novel first-in-class inhaled bifunctional compound possessing both muscarinic antagonist (MA) and β2-adrenoceptor agonist (BA) properties (MABA). In competition radioligand binding studies at human recombinant receptors, GSK-961081 displayed high affinity for hM2 (Ki = 1.4 nM), hM3 muscarinic receptors (Ki = 1.3 nM) and hβ2-adrenoceptors (Ki = 3.7 nM). GSK-961081 behaved as a potent hβ2-adrenoceptor agonist (EC50 = 0.29 nM for stimulation of cAMP levels) with 440- and 320-fold functional selectivity over hβ1- and hβ3-adrenoceptors, respectively. In guinea pig isolated tracheal tissues, GSK-961081 produced smooth muscle relaxation through MA (EC50 = 50.2 nM), BA (EC50=24.6 nM), and MABA (EC50 = 11 nM) mechanisms.

Reference: J Pharmacol Exp Ther. 2014 Oct;351(1):190-9. https://pubmed.ncbi.nlm.nih.gov/25100753/

In vivo activity

In the guinea pig bronchoprotection assay, inhaled GSK-961081 produced potent, dose-dependent inhibition of bronchoconstrictor responses via MA (ED50 = 33.9 µg/ml), BA (ED50 = 14.1 µg/ml), and MABA (ED50 = 6.4 µg/ml) mechanisms. Significant bronchoprotective effects of GSK-961081 were evident in guinea pigs via MA, BA, and MABA mechanisms for up to 7 days after dosing. The lung selectivity index of GSK-961081 in guinea pigs was 55- to 110-fold greater than that of tiotropium with respect to systemic antimuscarinic antisialagogue effects and was 10-fold greater than that of salmeterol with respect to systemic β2-adrenoceptor hypotensive effects. These preclinical findings studies suggest that GSK-961081 has the potential to be a promising next-generation inhaled lung-selective bronchodilator for the treatment of airway diseases, including chronic obstructive pulmonary disease.

Reference: J Pharmacol Exp Ther. 2014 Oct;351(1):190-9. https://pubmed.ncbi.nlm.nih.gov/25100753/