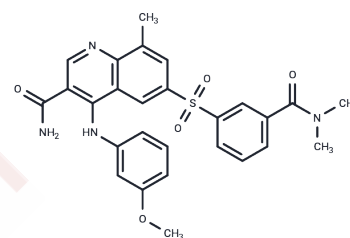


GSK256066

## Chemical Properties

CAS No. : 801312-28-7  
 Formula: C<sub>27</sub>H<sub>26</sub>N<sub>4</sub>O<sub>5</sub>  
 Molecular Weight: 518.58  
 Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year  
 Actual storage temperature shall be subject to the COA.



## Biological Description

|                             |   |
|-----------------------------|---|
| Description                 | GSK256066 is a selective PDE4B (equal affinity to isoforms A-D) inhibitor with IC <sub>50</sub> of 3.2 pM, >380,000-fold selectivity versus PDE1/2/3/5/6 and >2500-fold selectivity against PDE4B versus PDE7. Phase 2.   |
| Targets (IC <sub>50</sub> ) | PDE   |
| In vitro                    | GSK256066 is a slow and tight binding inhibitor of PDE4B with apparent IC <sub>50</sub> of 3.2 pM. GSK256066 is an extremely potent inhibitor of LPS-stimulated TNF $\alpha$ production in PBMCs with pIC <sub>50</sub> of 11.0 and IC <sub>50</sub> of 10 pM and human whole-blood cultures with pIC <sub>50</sub> of 9.90 and IC <sub>50</sub> of 126 pM. GSK256066 is highly selective for PDE4 (>3.8 x 10 <sup>5</sup> -fold versus PDE1, PDE2, PDE3, PDE5, and PDE6 and >2.5 x 10 <sup>3</sup> -fold against PDE7). GSK256066 inhibits PDE4 isoforms A-D with equal affinity. [1]  |
| In vivo                     | GSK256066 inhibits the LPS-induced pulmonary neutrophilia with an ED <sub>50</sub> of 1.1 $\mu$ g/kg, achieving maximal inhibition of 72% at 30 $\mu$ g/kg when given in the aqueous suspension. GSK256066 inhibits the LPS-induced pulmonary neutrophilia with ED <sub>50</sub> of 2.9 $\mu$ g/kg, achieving maximal inhibition of 62% when given in the dry powder formulation. GSK256066 shows a moderate plasma clearance of 39 ml/min/kg, a moderate volume of distribution of 0.8 L/kg, and a relatively short half-life of 1.1 hour in the male CD rat. [1] GSK256066 sustains at a high lung concentration of 2.6 $\mu$ g/g after intra-tracheal administration as an aqueous suspension at a dose of 30 $\mu$ g/kg in rats. [2] GSK256066 (10 $\mu$ g/kg) is administered intratracheally at different times (2, 6, 12, 18, 24, and 36 hours) before LPS administration, inhibiting LPS-Induced Pulmonary Neutrophilia in rat lipopolysaccharide (LPS)-induced models of acute pulmonary inflammation. GSK256066 (0.3–100 $\mu$ g/kg) inhibits LPS-induced increases in exhaled nitric oxide with ED <sub>50</sub> of 35 $\mu$ g/kg in rat. GSK256066 (10 $\mu$ g/kg) is administered half a hour before OVA administration in rat, inhibiting OVA-induced pulmonary eosinophilia with ED <sub>50</sub> of 0.4 $\mu$ g/kg. GSK256066 administered intratracheally as a dry powder blended in respiratory-grade lactose at doses of 3 to 100 $\mu$ g/kg 2 hours before inhaled LPS challenge in ferrets, inhibiting LPS-induced pulmonary neutrophilia with ED <sub>50</sub> of 18 $\mu$ g/kg without inducing emetic episodes. [3] |

## Solubility Information

## A DRUG SCREENING EXPERT

|            |  |
|------------|--|
| Solubility | DMSO: 10 mg/mL (19.28 mM), Sonication is recommended.<br>(< 1 mg/ml refers to the product slightly soluble or insoluble) |
|------------|--|

### Preparing Stock Solutions

|       | 1mg       | 5mg       | 10mg       |
|-------|-----------|-----------|------------|
| 1 mM  | 1.9283 mL | 9.6417 mL | 19.2834 mL |
| 5 mM  | 0.3857 mL | 1.9283 mL | 3.8567 mL  |
| 10 mM | 0.1928 mL | 0.9642 mL | 1.9283 mL  |
| 50 mM | 0.0386 mL | 0.1928 mL | 0.3857 mL  |

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

### Reference

- Tralau-Stewart CJ, et al. J Pharmacol Exp Ther, 2011, 337(1), 145-154.  
Woodrow MD, et al. Bioorg Med Chem Lett, 2009, 19(17), 5261-5265.  
Nials AT, et al. J Pharmacol Exp Ther, 2011, 337(1), 137-144.

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