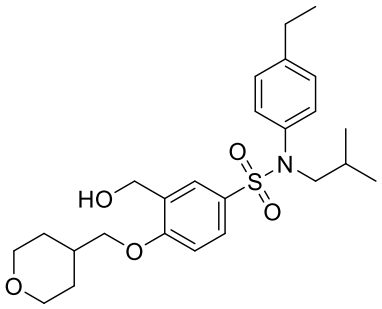
Product data sheet

MedKoo Cat#: 526931 Name: GSK2981278 CAS#: 1474110-21-8 Chemical Formula: $C_{25}H_{35}NO_5S$ Exact Mass: 461.2236 Molecular Weight: 461.62	
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:

GSK2981278 is a highly potent and selective inverse agonist of retinoic acid receptor-related orphan receptor gamma (ROR gamma). GSK2981278 is a strong RORγ-selective inverse agonist that inhibits activation of the il17 promoter. GSK2981278 robustly inhibits RORγ-mediated cytokine production at both the mRNA and protein level. GSK2981278 attenuates inflammation in a mouse model of psoriasis. Topical treatment with GSK2981278 will significantly limit Th17-type cytokine expression and should therefore lead to improved clinical outcomes for patients.

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	92	199.30
Ethanol	92	199.30

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.17 mL	10.83 mL	21.66 mL
5 mM	0.43 mL	2.17 mL	4.33 mL
10 mM	0.22 mL	1.08 mL	2.17 mL
50 mM	0.04 mL	0.22 mL	0.43 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. Smith SH, Peredo CE, Takeda Y, Bui T, Neil J, Rickard D, Millerman E, Therrien JP, Nicodeme E, Brusq JM, Birault V, Viviani F, Hofland H, Jetten AM, Cote-Sierra J. Development of a Topical Treatment for Psoriasis Targeting RORγ: From Bench to Skin. PLoS One. 2016 Feb 12;11(2):e0147979. doi: 10.1371/journal.pone.0147979. PMID: 26870941; PMCID: PMC4752338.

In vivo study

1. Smith SH, Peredo CE, Takeda Y, Bui T, Neil J, Rickard D, Millerman E, Therrien JP, Nicodeme E, Brusq JM, Birault V, Viviani F, Hofland H, Jetten AM, Cote-Sierra J. Development of a Topical Treatment for Psoriasis Targeting RORγ: From Bench to Skin. PLoS One. 2016 Feb 12;11(2):e0147979. doi: 10.1371/journal.pone.0147979. PMID: 26870941; PMCID: PMC4752338.

7. Bioactivity

Biological target:

GSK2981278 is a highly potent and selective inverse agonist for RORγ.

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In vitro activity

GSK2981278 markedly and potently inhibits IL-17A and IL-22 protein secretion in a concentration dependent manner (IC50 = 3.2 nM) during 5 days of culture under Th17 skewing conditions.GSK2981278 (0.3, 1, 3, 10, 30, 100, 300, 1000 pM; 5 day) potently and selectively inhibits IL-17 and IL-22 levels. Culture in the presence of ≥3 nM GSK2981278 led to a near-complete inhibition of IL-17A protein secretion.

Reference: PLoS One. 2016 Feb 12;11(2):e0147979. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/26870941/

In vivo activity

The imiquimod (IMQ) mouse model was employed to demonstrate efficacy of GSK2981278 in a psoriaform-like mouse model. Topical application of IMQ can induce and exacerbate psoriasis-like chronic skin inflammation in mice, including epidermal thickening, a dependence on T cell immunity, and a mechanism dependent on the IL-23/IL-17 pathway. It was first confirmed that GSK2981278 can inhibit IL-17A protein secretion by mouse CD4+ T cells, confirming cross-reactivity of our compound for both mouse and human RORγ (data not shown). Next, mice were treated topically with GSK2981278 (1% ointment or placebo) for three days (day -3 to day 0), after which mice continued to receive compound for the duration of the study. Starting on day 0, mice were challenged topically with IMQ (5%) cream or petrolatum (non-inflammatory inert cream) for up to ten days (day 0 to day +9). On the last day of treatment, the skin was imaged and clinically assessed. GSK2981278 was undetectable (<5 ng/ml) in serum at harvest, indicating that systemic exposure was minimal. Mice exposed to GSK2981278 exhibited reduced skin redness and scaling, as well as decreased hyperplasia, as evidenced by a 23% reduction in epidermal thickness when compared to the placebo + IMQ-treated group (Fig 2A and 2B).

Reference: PLoS One. 2016 Feb 12;11(2):e0147979. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/26870941/