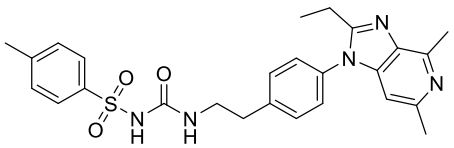
Product data sheet

MedKoo Cat#: 522545 Name: Grapiprant CAS#: 415903-37-6 Chemical Formula: $C_{26}H_{29}N_5O_3S$ Exact Mass: 491.1991 Molecular Weight: 491.61	
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:

Grapiprant, also known as CJ-023,423, RQ-00000007 and AAT-007, is a novel, potent and selective prostaglandin EP4 receptor antagonist with antihyperalgesic properties. In vitro, CJ-023,423 inhibits [(3)H]PGE(2) binding to both human and rat EP(4) receptors with K(i) of 13 +/- 4 and 20 +/- 1 nM, respectively. CJ-023,423 is highly selective for the human EP(4) receptor over other human prostanoid receptor subtypes. It also inhibits PGE(2)-evoked elevation in intracellular cAMP at the human and rat EP(4) receptors with pA(2) of 8.3 +/- 0.03 and 8.2 +/- 0.2 nM, respectively. In vivo, oral administration of CJ-023,423 significantly reduces thermal hyperalgesia induced by intraplantar injection of PGE(2) (ED(50) = 12.8 mg/kg).

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	30.0	61.02
DMF	20.0	40.68
DMF:PBS (pH 7.2) (1:3)	0.25	0.51
Ethanol	10.0	20.34

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.03 mL	10.17 mL	20.34 mL
5 mM	0.41 mL	2.03 mL	4.07 mL
10 mM	0.20 mL	1.02 mL	2.03 mL
50 mM	0.04 mL	0.20 mL	0.41 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. Nakao K, Murase A, Ohshiro H, Okumura T, Taniguchi K, Murata Y, Masuda M, Kato T, Okumura Y, Takada J. CJ-023,423, a novel, potent and selective prostaglandin EP4 receptor antagonist with antihyperalgesic properties. J Pharmacol Exp Ther. 2007 Aug;322(2):686-94. doi: 10.1124/jpet.107.122010. Epub 2007 May 10. PMID: 17495127.

In vivo study

1. Rausch-Derra L, Huebner M, Wofford J, Rhodes L. A Prospective, Randomized, Masked, Placebo-Controlled Multisite Clinical Study of Grapiprant, an EP4 Prostaglandin Receptor Antagonist (PRA), in Dogs with Osteoarthritis. J Vet Intern Med. 2016 May;30(3):756-63. doi: 10.1111/jvim.13948. Epub 2016 Apr 13. PMID: 27075237; PMCID: PMC4913586.

2. Kirkby Shaw K, Rausch-Derra LC, Rhodes L. Grapiprant: an EP4 prostaglandin receptor antagonist and novel therapy for pain and inflammation. Vet Med Sci. 2015 Dec 21;2(1):3-9. doi: 10.1002/vms3.13. PMID: 29067176; PMCID: PMC5645826.

7. Bioactivity

Biological target:

Grapiprant (CJ-023423) is a selective EP4 receptor antagonist whose physiological ligand is prostaglandin E2 (PGE2). Grapiprant displaces [^{3}H]-PGE2 (1 nM) binding to dog recombinant EP4 receptor with IC50 value of 35 nM and Ki value of 24 nM.

In vitro activity

PGE2 dose-dependently increased intracellular cAMP accumulation at human EP4 receptors expressed in HEK293 cells. Increasing concentrations of CJ-023,423 produced a rightward shift in the concentration-response curve for PGE2 without modulating the maximal cAMP production (Fig. 3A). The pA2 value was calculated as 8.3 ± 0.03 with a slope of 1.3 ± 0.1 (n = 3) by Schild plot analysis . These experiments were repeated using HEK293 cells transfected with cDNA encoding the rat EP4 receptor, resulting in a pA2 value of 8.2 ± 0.2 with a slope of 1.2 ± 0.1 (n = 4) (Fig. 3B). CJ-023,423 did not show any agonist activity at the human and rat recombinant EP4 receptors (data not shown). These data suggest that CJ-023,423 is a competitive antagonist at the human and rat EP4 receptors.

Reference: J Pharmacol Exp Ther. 2007 Aug;322(2):686-94. https://jpet.aspetjournals.org/content/322/2/686.long

In vivo activity

This randomized, placebo-controlled masked study of a prostaglandin EP4 receptor antagonist for the control of pain and inflammation in dogs with OA (osteoarthritis) showed that grapiprant treatment resulted in a significant number of dogs with decreased PSS and PIS, as evaluated by the owner, and a decrease in the TOS, as evaluated by the veterinarian. In addition, grapiprant used for 28 days in this population of dogs was found to be safe. Adverse events were relatively mild and of short duration. No dog was withdrawn from the study, despite a higher frequency of transient vomiting in the grapiprant-treated dogs. These findings are important because grapiprant represents the first approach to daily PO treatment of pain and inflammation in dogs with OA with a mechanism of action targeted to binding and antagonizing a prostaglandin receptor (EP4) rather than inhibiting cyclooxygenase enzymes.

Reference: J Vet Intern Med. 2016 May-Jun; 30(3): 756–763. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4913586/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.