Product Data Sheet

Product Name: PF-03394197(Oclacitinib)
Cat. No.: GC14938

Chemical Properties

Cas. No.	1208319-26-9		
Chemical Name	N-methyl-1-((1r,4r)-4-(methyl(7H-pyrrolo[2,3-d]pyrimidin-4-yl)amino)cyclohexyl)methanesulfonamide		
SMILES	CNS(C[C@@]1([H])CC[C@@](N(C2=NC=NC3=C2C=CN3)C)([H])CC1)(=O)=O		
Formula	$C_{15}H_{23}N_5O_2S$	M.Wt	337.44
Solubility	≥ 33.7mg/mL in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ 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	PF-03394197(Oclacitinib)		

Protocol

Kinase experiment:	Recombinant human active kinase domains for JAK1, JAK2, JAK3, and TYK2 are used in isolated enzyme assays using Caliper microfluidics technology to determine potency of Oclacitinib against the JAK family members. Sequence homology to the analogous sequences in the canine JAK enzymes are 98, 98, 100, and 90%, respectively. Invitrogen kinase panel testing is performed to determine potency of Oclacitinib toward 38 different non-JAK kinases using their SelectScreen Kinase Profiling Services. Oclacitinib is evaluated at a concentration of 1 μM[1].

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Animal experiment:

Mice[2]BALB/cAnN (female, 6 weeks old) are used. The JAK inhibitors (Tofacitinib or Oclacitinib) are administered orally or topically 30 minutes before and 4 hours after toluene-2,4-diisocyanate (TDI) challenge because the absorption of Tofacitinib and Oclacitinib is rapid, with plasma concentrations for both Tofacitinib and Oclacitinib peaking at around 1 hour after oral or intravenous administration. Tofacitinib and Oclacitinib both have a short half-life of 2 and 4 hours after administration, respectively. Each drug is diluted in a 0.5% methylcellulose/0.25% Tween 20 solution for oral administration, and a 7:1 acetone:DMSO solution for topical application to concentrations described subsequently. For each drug, a vehicle-only control group and low- and high-dose groups are set. Oral doses are as follows: Tofacitinib, 10 and 30 mg/kg; and Oclacitinib, 30 and 45 mg/kg. Topically administered doses are 0.1, 0.25, and 0.5% for both chemicals. The oral doses of Tofacitinib and Oclacitinib used in this study are selected.Dogs[3]Dogs are randomized to one of two treatment groups (i.e. Oclacitinib or placebo) in a 1:1 ratio. Dogs in the Oclacitinib treatment group are given Oclacitinib maleate caplets orally at a dose of 0.4-0.6 mg/kg twice daily. The scored caplets are provided in three strengths containing 3.6, 5.4 and 16 mg of Oclacitinib. Dogs in the placebo treatment group are given the same number of caplets, identical in appearance to Oclacitinib maleate caplets and containing all of the same excipients except Oclacitinib maleate.

References:

[1]. Gonzales AJ, et al. Oclacitinib (APOQUEL) is a novel Janus kinase inhibitor with activity

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against cytokines involved in allergy. J Vet Pharmacol Ther. 2014 Aug;37(4):317-24.
[2]. Fukuyama T, et al. Topically Administered Janus-Kinase Inhibitors Tofacitinib and Oclacitinib Display Impressive Antipruritic and Anti-Inflammatory Responses in a Model of Allergic Dermatitis. J Pharmacol Exp Ther. 2015 Sep;354(3):394-405.
[3]. Cosgrove SB, et al. Efficacy and safety of oclacitinib for the control of

pruritus and associated skin lesions in dogs with canine allergic dermatitis. Vet Dermatol. 2013 Oct;24(5):479-e114.

Background

Description:

IC50: 10 nM for JAK1

Janus kinase (JAK) enzymes are involved in cell signaling pathways activated by cytokines dysregulated in allergy. PF-03394197 (Oclacitinib) is a novel Janus kinase inhibitor.

In vitro: PF-03394197 inhibited JAK family members by 50% at concentrations ranging from 10 to 99 nM and did not inhibit a panel of 38 non-JAK kinases. PF-03394197 was most potent at inhibiting JAK1. PF-03394197 also inhibited the function of JAK1-dependent cytokines involved in allergy and inflammation as well as pruritus. PF-03394197 had minimal effects on cytokines which did not activate the JAK1 enzyme in cells [1].

In vivo: PF-03394197 administered orally at a dose of 0.4–0.6 mg/kg twice daily was safe and efficacious in controlling the pruritus associated with allergic dermatitis. PF-03394197 provided itch relief within 24 h that persisted through the treatment period, with over 70% of the treated dogs achieving a >50% reduction in pruritus by day 7 [2].

Clinical trial: PF-03394197 (Oclacitinib) (APOQUEL?) has recently been approved in the United States and European Union for the control or treatment of pruritus associated with allergic dermatitis and the control or treatment of AD in dogs [1].

Reference:
[1] Gonzales AJ, Bowman JW, Fici GJ, Zhang M, Mann DW, Mitton-Fry M. Oclacitinib

(APOQUEL(?)) is a novel Janus kinase inhibitor with activity against cytokines involved in allergy. J Vet Pharmacol Ther. 2014 Aug;37(4):317-24.
[2] Cosgrove SB, Wren JA, Cleaver DM, Martin DD, Walsh KF, Harfst JA, Follis SL, King VL, Boucher JF, Stegemann MR. Efficacy and safety of oclacitinib for the control of pruritus and associated skin lesions in dogs with canine allergic dermatitis. Vet Dermatol. 2013 Oct;24(5):479-e114.