

Product Data Sheet

Product Name: CCX140
Cat. No.: GC31330

Chemical Properties

Cas. No. 1100318-47-5

SMILES FC(F)(F)C1=CC(S(=O)(=O)NC2=CC(C)=CN=C2C(C3=NC=NC4=C3C=CN4)=O)=O)=CC=C1Cl

Formula $C_{20}H_{13}ClF_3N_5O_3S$ M.Wt 495.86

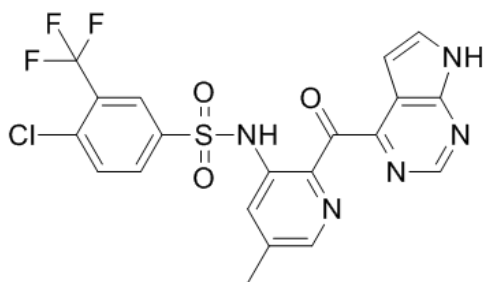
Solubility DMSO: ≥ 100 mg/mL (201.67 mM);
Water: 0.25 mg/mL (0.50 mM and warming)

Storage Store at -20°C, protect from light

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C 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



Protocol

Caution: Product has not been fully validated for medical applications. For research use only.

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Animal experiment: Mice: CCX140 is formulated as a solution in 1% hydroxypropyl methylcellulose. Male uninephrectomized hCCR2 KI mice are rendered diabetic with the high-fat diet and dosed with 100 mg/kg CCX140, but for 8 wk of dosing. Eight-week-old male hCCR2 KI Lepr db/db mice are similarly dosed with 100 mg/kg CCX140 for 6 wk[1].

References:

- [1]. Sullivan T, et al. CCR2 antagonist CCX140-B provides renal and glycemic benefits in diabetic transgenic human CCR2 knockin mice. *Am J Physiol Renal Physiol*. 2013 Nov 1;305(9):F1288-97.
[2]. Sullivan TJ, et al. Experimental evidence for the use of CCR2 antagonists in the treatment of type 2 diabetes. *Metabolism*. 2013 Nov;62(11):1623-32.

Background

CCX140 is a potent CCR2 antagonist.

CCX140-B potently inhibits CCL2-induced chemotaxis of purified human blood monocytes with IC₅₀ values of 8 nM in buffer and 200 nM in the presence of 100% human serum. CCX140-B also inhibits CCL2-induced Ca²⁺ mobilization in monocytes with an IC₅₀ value of 3 nM. CCX140-B inhibits the binding of 125I-CCL2 to monocytes with an IC₅₀ value of 17 nM. CCX140-B has a K_d value of 2.3 nM toward hCCR2. CCX140-B also inhibits monocyte chemotaxis mediated by the other CCR2 ligands: CCL8/MCP-2, CCL7/MCP-3, and CCL13/MCP-4[1].

Treatment of hCCR2 KI mice with CCX140-B causes a dose-dependent reduction in the number of peritoneal leukocytes after thioglycollate challenge: CCX140-B strongly blocks leukocyte infiltration at 30 mg/kg, partially blocks leukocyte infiltration at 10 mg/kg, and fails to block leukocyte infiltration at 3 mg/kg. In DIO hCCR2 KI mice, treatment with 100 mg/kg CCX140-B blocks the progressive increase in UAER and ACR. CCX140-B maintains lower UAER and ACR values during the entire 8-wk dosing regimen[1]. In DIO mice, the CCR2 antagonist completely blocks the recruitment of inflammatory macrophages to visceral adipose tissue. The mice exhibit reduced hyperglycemia and insulinemia, improved insulin sensitivity, increased circulating adiponectin levels, decreased pancreatic islet size and increased islet number. It also reduces urine output, glucose excretion, hepatic glycogen and triglyceride content and glucose 6-phosphatase levels[2].

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