SZABO SCANDIC

Part of Europa Biosite

# Produktinformation

- Forschungsprodukte & Biochemikalien
- Zellkultur & Verbrauchsmaterial
- Diagnostik & molekulare Diagnostik
- Laborgeräte & Service

Weitere Information auf den folgenden Seiten!
See the following pages for more information!

## Lieferung & Zahlungsart

siehe unsere Liefer- und Versandbedingungen

## Zuschläge

- Mindermengenzuschlag
- Trockeneiszuschlag
- Gefahrgutzuschlag
- Expressversand


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# Avacopan

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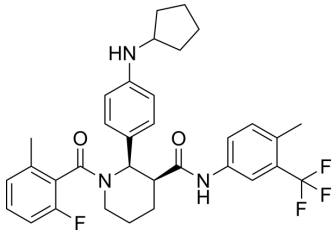
| **Cat. No.:** | HY-17627 |
| **CAS No.:** | 1346623-17-3 |
| **Molecular Formula:** | $C_{33}H_{35}F_4N_3O_2$ |
| **Molecular Weight:** | 581.64 |
| **Target:** | Complement System |
| **Pathway:** | Immunology/Inflammation |
| **Storage:** | Powder -20°C 3 years<br>4°C 2 years<br>In solvent -80°C 6 months<br>-20°C 1 month |



## SOLVENT & SOLUBILITY

**In Vitro**

DMSO : ≥ 10.1 mg/mL (17.36 mM)

* "≥" means soluble, but saturation unknown.

**Preparing Stock Solutions**

| Solvent / Mass / Concentration | 1 mg | 5 mg | 10 mg |
|---|---|---|---|
| 1 mM | 1.7193 mL | 8.5964 mL | 17.1928 mL |
| 5 mM | 0.3439 mL | 1.7193 mL | 3.4386 mL |
| 10 mM | 0.1719 mL | 0.8596 mL | 1.7193 mL |

Please refer to the solubility information to select the appropriate solvent.

## BIOLOGICAL ACTIVITY

**Description**

Avacopan (CCX168) is a potent, selective and orally available complement 5a receptor (C5aR) inhibitor with an $IC_{50}$ of 0.1 nM.

**$IC_{50}$ & Target**

IC50: 0.1 nM (complement 5a receptor )[1]

**In Vitro**

CCX168 displaces [$^{125}$I]-C5a binding to C5aR on a human myeloid cell line (U937) with a potency ($IC_{50}$) of 0.1 nM. CCX168 inhibits C5a-mediated chemotaxis of U937 cells with a potency (the concentration of CCX168 that produces a 2-fold right-shift in C5a activity) of 0.2 nM. CCX168 competitively and selectively blocked C5a-induced calcium mobilization in purified human neutrophils, with an $IC_{50}$ value of 0.2 nM. CCX168 inhibited C5a-induced release of reactive-oxygen species from isolated neutrophils, and is able to completely block respiratory burst in these neutrophils[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

**In Vivo**

CCX168 is shown to be well tolerated across a broad dose range (1 to 100 mg) and it showed dose-dependent pharmacokinetics. An oral dose of 30 mg CCX168 given twice daily blocked the C5a-induced upregulation of CD11b in

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| | circulating neutrophils by 94% or greater throughout the entire day, demonstrating essentially complete target coverage. In mice dosed orally with 0.03 mg/kg of CCX168, the resulting plasma CCX168 concentration of 15 nM (8.7 ng/mL) reduces the drop in circulating leukocytes from 53% to 25%. In mice administered 0.3 mg/kg of CCX168, the resulting plasma CCX168 concentration of 75 nM (44 ng/mL) reduces the drop in circulating leukocytes from 53% to only 10% relative to baseline ($p<0.05$ for CCX168 vs. vehicle control). Oral doses of CCX168 of either 3 or 30 mg/kg completely blocks C5a-induced leukopenia in hC5aR knock-in mice[1].? Oral CCX168, 30 mg/kg daily, reduces the severity of anti-MPO NCGN in hC5aR mice. Glomerular crescents are reduced from 30.4% to 3.3% with CCX168. Urine hematuria, proteinuria, and leukocyturia are reduced in mice receiving CCX168, 30 mg/kg per day. The protection by CCX168 results in reduced crescents and necrosis[2].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |

## PROTOCOL

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| **Animal Administration** [1] | Mice: Human C5aR knock-in mice are dosed with vehicle (PEG-400/solutol-HS15 70:30, 5 mL/kg) or CCX168 by oral gavage. One hour after dosing, C5a (20 μg/kg, 0.1 mL dose volume) is injected intravenously and blood samples collected from retro-orbital eye bleeds. Blood leukocyte levels are analyzed by flow cytometry[1].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |

## CUSTOMER VALIDATION

- Cell. 2023 Jun 22;186(13):2802-2822.e22.

See more customer validations on www.MedChemExpress.com

## REFERENCES

[1]. Bekker P, et al. Characterization of Pharmacologic and Pharmacokinetic Properties of CCX168, a Potent and Selective Orally Administered Complement 5a Receptor Inhibitor, Based on Preclinical Evaluation and Randomized Phase 1 Clinical Study. PLoS One. 2016 Oct 21;11(10):e0164646.

[2]. Xiao H, et al. C5a receptor (CD88) blockade protects against MPO-ANCA GN. J Am Soc Nephrol. 2014 Feb;25(2):225-31.



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