# TAK-220

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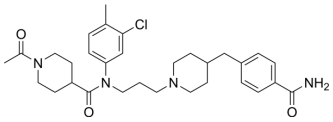
|---|---|
| **Cat. No.:** | HY-19974 |
| **CAS No.:** | 333994-00-6 |
| **Molecular Formula:** | $C_{31}H_{41}ClN_4O_3$ |
| **Molecular Weight:** | 553.14 |
| **Target:** | CCR; HIV |
| **Pathway:** | GPCR/G Protein; Immunology/Inflammation; Anti-infection |
| **Storage:** | Powder -20°C 3 years<br>4°C 2 years<br>In solvent -80°C 6 months<br>-20°C 1 month |



## SOLVENT & SOLUBILITY

**In Vitro**

DMSO : ≥ 50 mg/mL (90.39 mM)

* "≥" means soluble, but saturation unknown.

| Preparing Stock Solutions | Concentration / Solvent / Mass | 1 mg | 5 mg | 10 mg |
|---|---|---|---|---|
| | 1 mM | 1.8079 mL | 9.0393 mL | 18.0786 mL |
| | 5 mM | 0.3616 mL | 1.8079 mL | 3.6157 mL |
| | 10 mM | 0.1808 mL | 0.9039 mL | 1.8079 mL |

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

**In Vivo**

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (4.52 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.52 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.52 mM); Clear solution

## BIOLOGICAL ACTIVITY

**Description**

TAK-220 is a selective and orally bioavailable CCR5 antagonist, with $IC_{50}$s of 3.5 nM and 1.4 nM for inhibition on the binding of RANTES and MIP-1α to CCR5, respectively, but shows no effect on the binding to CCR1, CCR2b, CCR3, CCR4, or CCR7; TAK-220 also selectively inhibits HIV-1, with $EC_{50}$s of 1.2 nM (HIV-1 KK), 0.72 nM (HIV-1 CTV), 1.7 nM (HIV-1 HKW), 1.7 nM (HIV-1 HNK), 0.93 nM (HIV-1 HTN), and 0.55 nM (HIV-1 HHA), and $EC_{90}$s of 12 nM (HIV-1 KK), 5 nM (HIV-1 CTV), 12 nM (HIV-1 HKW), 28 nM (HIV-1 HNK), 15 nM (HIV-1 HTN), and 4 nM (HIV-1 HHA) in PBMCs.

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| **$IC_{50}$ & Target** | MIP-1α-CCR5<br>1.4 nM ($IC_{50}$, in CHO cells) | RANTES-CCR5<br>3.5 nM ($IC_{50}$, in CHO cells) | HIV-1 (HHA)<br>0.55 nM (EC50, in PBMCs) | HIV-1 (CTV)<br>0.72 nM (EC50, in PBMCs) |
| | HIV-1 (HTN)<br>0.93 nM (EC50, in PBMCs) | HIV-1 (KK)<br>1.2 nM (EC50, in PBMCs) | HIV-1 (HKW)<br>1.7 nM (EC50, in PBMCs) | HIV-1 (HNK)<br>1.7 nM (EC50, in PBMCs) |
| | HIV-1 (HHA)<br>4 nM (EC90, in PBMCs) | HIV-1 (CTV)<br>5 nM (EC90, in PBMCs) | HIV-1 (KK)<br>12 nM (EC90, in PBMCs) | HIV-1 (HKW)<br>12 nM (EC90, in PBMCs) |
| | HIV-1 (HTN)<br>15 nM (EC90, in PBMCs) | HIV-1 (HNK)<br>28 nM (EC90, in PBMCs) | | |

**In Vitro**

TAK-220 is a selective CCR5 antagonist, with $IC_{50}$s of 3.5 nM and 1.4 nM for inhibition on the binding of RANTES and MIP-1α to CCR5 in CHO cells, respectively, but shows no effect on the binding to CCR1, CCR2b, CCR3, CCR4, or CCR7. TAK-220 (0-1000 nM) interacts with CCR5 but not with RANTES and inhibits the CCR5-mediated Casup>2+ signaling. TAK-220 inhibits R5 HIV-1 (JR-FL) envelope-mediated membrane fusion, with an $IC_{50}$ value of 0.42 nM, but does not alter X4 HIV-1 (HXB2) envelope-mediated membrane fusion. TAK-220 also selectively inhibits HIV-1, with $EC_{50}$s of 1.2 nM (HIV-1 KK), 0.72 nM (HIV-1 CTV), 1.7 nM (HIV-1 HKW), 1.7 nM (HIV-1 HNK), 0.93 nM (HIV-1 HTN), and 0.55 nM (HIV-1 HHA), and $EC_{90}$s of 12 nM (HIV-1 KK), 5 nM (HIV-1 CTV), 12 nM (HIV-1 HKW), 28 nM (HIV-1 HNK), 15 nM (HIV-1 HTN), and 4 nM (HIV-1 HHA) in PBMCs[1]. TAK-220 shows potent inhibitory activity against the R5 isolates, with $IC_{50}$s of 3.12 nM against HIV-1 R5-08, 13.47 nM against HIV-1 R5-06, and 2.26 nM against HIV-1 R5-18. TAK-220 (>100 nM) has no toxicity in uninfected PBMCs[2].

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

## PROTOCOL

**Cell Assay [1]**

PHA-stimulated PBMCs are inoculated with 1,000 to 1,400 CCID50s of R5 HIV-1 (JR-FL) or X4 HIV-1 (IIIB) or with 13 to 55 ng of p24 of HIV-1 clinical isolates per $4 \times 10^6$ cells and incubated for 4 h. The cells are washed to remove unadsorbed viral particles and seeded into a 96-well plate ($2 \times 10^5$ cells/well) with culture medium containing various concentrations of TAK-220. The effects of high concentrations of human serum (HS) on the anti-HIV-1 activity of TAK-220 are examined with RPMI 1640 medium supplemented with either 20% FBS alone or 40% human type AB serum plus 10% FBS, 100 U/mL recombinant human interleukin 2, and antibiotics. On day 4 after infection, the cells are subcultured at 1:2 with culture medium containing the same concentrations of the test compounds. On day 7 after infection, the culture supernatants are collected and their p24 antigen levels are determined with a p24 antigen enzyme-linked immunosorbent assay kit[1].

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## CUSTOMER VALIDATION

- Bioact Mater. 2021 Jan 7;6(7):2039-2057.

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## REFERENCES

[1]. Takashima K, et al. Highly potent inhibition of human immunodeficiency virus type 1 replication by TAK-220, an orally bioavailable small-molecule CCR5 antagonist. Antimicrob Agents Chemother. 2005 Aug;49(8):3474-82.

[2]. Tremblay CL, et al. TAK-220, a novel small-molecule CCR5 antagonist, has favorable anti-human immunodeficiency virus interactions with other antiretrovirals in vitro. Antimicrob Agents Chemother. 2005 Aug;49(8):3483-5.

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

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